

Proceedings of the British Cardiac Society

THE 65TH ANNUAL GENERAL MEETING of the British Cardiac Society was held at the University of York on Wednesday and Thursday, 2 and 3 April 1986. The President, D G JULIAN, took the Chair during private business.

The following were elected to the British Cardiac Society.

New Ordinary Members: J Bayliss (Buckinghamshire); R M Bini (Liverpool); R S Clark (Dundee); A J Cowley (Nottinghamshire); P A Crean (London); J C P Crick (London); W Culling (Bristol); K D Dawkins (London); A Fenech (Glasgow); T H Foley (Surrey); C J Foster (Manchester); K A A Fox (Cardiff); A G Fraser (Glamorgan); D J M Keenan (Manchester); C A Kekwick (Devon); J N Leverment (Leicester); P Lynch (Hampshire); D G McDevitt (Dundee); C G A McGregor (Newcastle); B Mittra (Sunderland); O J M Ormerod (Cambridge); W J Penny (Cardiff); J W Pidgeon (Merseyside); A P Rae (Glasgow); D R Ramsdale (Merseyside); M R Rees (Leeds); C J Reid (London); E Rowland (London); J M Rowley (Nottinghamshire); S Saltissi (Liverpool); M Varma (Fermanagh).

New Corresponding Member: K I Shine (Los Angeles).

New Extraordinary Members: J M Barber, H H Bentall, J F Goodwin, C B Henderson, D Mendel, E G Wade, W Whitaker.

Resignations: K Bloor, I M Hill, F S Jackson, R B Milstein.

Death: F Szekely.

Elections

E Sowton, President-Elect; J Coltart elected Secretary; D J Parker elected Treasurer; R H Swanton elected Assistant Secretary; M Joy and T Treasure elected to Council.

Abstracts of papers

Arrhythmias before and after anatomical correction of transposition of the great arteries

R Martin, Rosemary Radley-Smith, M H Yacoub
Harefield Hospital, Harefield, Middlesex

Ninety two patients were studied after anatomical correction of transposition of the great arteries. Fifty four patients underwent primary correction, and 38 patients had two stage correction. Forty one patients had 24 hour ambulatory electrocardiograph recordings performed before any operative procedure. Thirty four (83%) patients showed sinus rhythm alone, one (2.4%) showed infrequent supraventricular extrasystoles, one (2.4%) showed a short episode of atrial fibrillation, five (12.2%) showed modified Lown grade 1 ventricular extrasystoles, and one (2.4%) showed an episode of ventricular tachycardia. Thirty one recordings in 20 patients after the first stage of a two stage repair showed no significant change in the frequency of any arrhythmias. No cases of late symptomatic arrhythmia or arrhythmia associated death occurred during a mean of 3.1 years follow up. Recordings immediately before discharge from hospital were performed in 47 patients. Supraventricular extrasystoles were seen in 13 (28%) patients and ventricular extrasystoles in 20 (42.5%), of which 14 (29.8%) were Lown grade 1 and six (12.8%) were Lown grade 3. One patient was in atrial fibrillation and one had paroxysmal atrial flutter. The latter patients required short term treatment with amiodarone. Sixty five recordings in 56 patients between three and 60 months after correction have demonstrated a low incidence of serious arrhythmias—38 (58%) showed sinus rhythm alone, 16 (25%) infrequent supraventricular extrasystoles, and 13 (20%) ventricular extrasystoles (11 Lown grade 1, one grade 3, and one grade 4). One early patient developed complete heart block post-operatively. In conclusion, there is a low incidence of important arrhythmias and late death after anatomical correction.

Natural history and prognosis of fetal tachycardias

E J Ladusans, Dianne Crawford, Lindsey Allan, M Tynan, P V L Curry
Guy's Hospital, London

Fetal tachycardia was diagnosed by echocardiography in 13 patients who have now been followed up for a mean of 2.9 years (range 1.1–3.8). Average gestational age at diagnosis was 35 weeks (range 32–38). Atrial flutter (AF) was found in six patients (four with hydrops fetalis), atrial tachycardia (AT) in two, and paroxysmal supraventricular tachycardia (SVT) in five (two hydropic). Cardiac structure was normal in all cases. To control ventricular rate (that is, below 200 beats/min) 11 received prenatal treatment with digoxin and two of these required verapamil in addition. One neonate with severe hydrops and SVT died shortly after premature delivery at 36 weeks, despite postnatal attempts to control tachycardia. All patients were treated with digoxin at birth. All six with AF reverted to sinus rhythm (five before delivery) and this has been maintained. In four children with AF, treatment has been withdrawn without relapse (shortest follow up 3.1 years). Amiodarone was used successfully to control refractory AT in one baby; unfortunately she died at 2 years from pneumococcal meningitis. Digoxin was withdrawn from the other child with AT, who has now been free from attacks for 3.2 years. Of four children with SVT, treatment has been stopped without recurrence of tachycardia in two. Two children remain on digoxin; one required the addition of verapamil to control breakthrough SVT, the other is symptom free (at 2.6 and 1.6 years respectively). Aggressive intrauterine treatment of fetal tachycardia may prevent fetal hydrops, premature delivery, and neonatal death. The prognosis for rhythm control after birth is excellent.

Ventricular septal defect and pulmonary hypertension (PHT): a long term follow up study

K A Hallidie-Smith
Royal Postgraduate Medical School, London

To assess the long term efficacy of closure of ventricular septal defect (VSD) with PHT, 27 patients who were aged 3–12 years at operation were followed up for 19–27 years. All had large VSD, systemic level pulmonary artery pressure, and an overall left to right shunt, and 25 had a pulmonary arteriolar resistance of ≥ 8 units. All patients were repeatedly examined clinically and by ECG and chest x ray and had at least two postoperative cardiac catheterisations with measurement of pulmonary arteriolar pressure at rest and on effort. Most patients

had respiratory function tests, two stage exercise testing, 24 hour Holter monitoring, and cross sectional echocardiograms. In 1975 all were symptom free, very active, and had normal respiratory and exercise tests. However, only four had normal resting pulmonary artery pressure and in 16/16 this was abnormally raised on effort. By 1985 six patients had died (aged 17–32 years, and 14–21 years after operation) and three patients had symptoms. The other patients were symptom free and two women had children. The patients died in severe right heart failure within five years of first symptoms. Increasing heart size on chest x ray and cross sectional echocardiographic evidence of right ventricular dilatation and pressure overload were bad prognostic features preceding symptoms. Predictably the patients who died had severe PHT; however, three patients with severe PHT remain symptom free.

The patients had an excellent quality of life while they were symptom free but rapidly deteriorated once symptoms developed. The group as a whole may not be living as long as reported cases of Eisenmenger syndrome. In many cases pulmonary vascular disease appeared to continue to progress post-operatively in these patients who were all over two years of age when their large VSD was closed.

Membranous supravulvar mitral stenosis: a potentially curable form of congenital heart disease

I D Sullivan, P J Robinson, M R de Leval,
F J Macartney, T P Graham Jr
The Hospital for Sick Children, Great Ormond
Street, London

Failure to differentiate membranous supravulvar mitral stenosis from isolated mitral valve stenosis may result in undue delay of operation because the likelihood of mitral valve replacement is high in mitral valve stenosis. Fourteen patients who had operation for membranous supravulvar mitral stenosis between 1978–85 were reviewed in an attempt to clarify specific echocardiographic features which might facilitate early diagnosis. Ages ranged from six weeks to 13 years. Associated lesions included ventricular septal defect (7), left superior vena cava (6), coarctation (5), subaortic stenosis (3), and atrial septal defect (1). Twelve patients had the membrane excised, and two patients with associated mitral valve stenosis required valve replacement. There were no operative deaths. Review of preoperative cross sectional echocardiograms which were avail-

able in 11 patients allowed retrospective diagnosis of membranous supralvalvar mitral stenosis in 10 patients. Membranous supralvalvar mitral stenosis had been recognised in only five of these pre-operatively. There were two types of membranous supralvalvar mitral stenosis: in seven patients the membrane was adherent to the valve and visible only in isolated diastolic frames. In the second type (three patients) there was clear separation between the membrane and valve leaflets in diastolic frames with systolic apposition of the valve leaflets and the membrane. Of 11 patients followed for > 1 year nine are alive. Eight are symptom free and seven have no evidence of left ventricular inflow obstruction. Patients with evidence of left ventricular inflow obstruction should have extensive cross sectional echocardiographic evaluation to detect membranous supralvalvar mitral stenosis which may be amenable to operation without valve replacement.

Chronic enalapril treatment reduces myocardial noradrenaline response to exercise in heart failure

I P Mulligan, A G Fraser, V G Tirlapur, M J Lewis, A H Henderson
University of Wales College of Medicine, Cardiff

In congestive heart failure exercise tolerance and mortality are related to sympathetic activity. Angiotensin converting enzyme inhibitors may reduce the arrhythmias which contribute to mortality, perhaps by reducing sympathetic drive as reflected by plasma noradrenaline concentrations or myocardial noradrenaline release. The effects of treatment for six weeks with enalapril (20 mg/day) or placebo were investigated in a double blind crossover study of 14 men with congestive heart failure refractory to continuing digoxin and diuretic treatment. Eleven had ischaemic heart disease and three had congestive cardiomyopathy; the radionuclide ejection fraction was 20 (2) (mean (SE)). Exercise tolerance was assessed by the symptom limited duration of a standard protocol bicycle test. At peak exercise, enalapril compared with placebo reduced myocardial noradrenaline release by 88% from 92.5 (40.2) ng/min ($p < 0.05$), arterial noradrenaline by 3% from 1345 (187) pg/ml (NS), and coronary sinus flow by 16% from 240 (22) ml/min (NS). At rest, enalapril reduced these variables respectively by 55% from 20.2 (22.6) ng/min, by 1% from 871 (222) pg/ml, and by 6% from 142 (14) ml/min (all NS). Exercise tolerance was not significantly altered (-6% from

615 (77)s), but the double product at peak exercise was reduced by 21% from 21 292 (1758) mm Hg/s ($p < 0.05$). Transmyocardial arteriovenous oxygen difference was reduced by 12% from 14.2 (0.6) ml/dl ($p < 0.05$) and myocardial oxygen consumption by 26% from 35.2 (5.0) ml/min (NS).

This study provides direct evidence that chronic enalapril treatment reduces myocardial sympathetic stimulation during exercise in association with reduced myocardial workload.

Haemodynamic effects of frusemide in the presence and absence of angiotensin converting enzyme inhibitors

J G F Cleland, G Gillen, H J Dargie
Cardiac Department, Western Infirmary, Glasgow

Angiotensin converting enzyme (ACE) inhibitors are usually prescribed with diuretics in patients with heart failure yet little is known about their interaction especially in relation to renal and cardiac function. We measured glomerular filtration rate (GFR), renal blood flow, and plasma volume radioisotopically, cardiac output by Doppler echocardiography, and serum and urine composition over six hour periods in twelve patients with cardiac failure on a fixed sodium and potassium intake, before and after frusemide (80 to 120 mg) and after one week of enalapril 10 mg daily. Enalapril alone increase cardiac output (3.0 (1) to 3.4 (1) l/min; $p < 0.05$) and reduced mean blood pressure slightly (90 (5) to 85 (4) mm Hg; $p < 0.01$). Renal blood flow rose (424 (202) to 494 (225) ml/min; $p < 0.08$) but GFR did not change (70 (27) and 69 (27) ml/min); consequently the filtration fraction fell (33 (14) to 26 (6)%; $p < 0.05$). With frusemide the addition of enalapril also increased cardiac output (3.1 (1.1) to 3.6 (1.0) l/min; $p < 0.01$) and reduced blood pressure (87 (5) to 79 (4) mm Hg; $p < 0.001$). Renal blood flow increased to a greater extent (463 (216) to 579 (211) ml/min; $p < 0.02$) but GFR declined (70 (27) to 63 (26) ml/min; $p < 0.001$) so that the filtration fraction fell markedly (30 (9) to 19 (5)%; $p < 0.001$). Enalapril without frusemide had no effect on urine volume but reduced the diuretic response to frusemide from 1.21 per 6 hours to 0.81 ($p < 0.001$). Plasma volume increased (3.4 to 3.7 l; $p < 0.02$) and body weight by 1.2 (0.5) kg over the one week treatment period. Enalapril inhibited the increases in angiotensin II, aldosterone, and noradrenaline induced by frusemide. ACE inhibitors appear to unmask the renal vasodilator effects of frusemide.

The reduced filtration fraction suggests that the increase in renal blood flow after ACE inhibitors is due to a reduction in angiotensin II mediated efferent arteriolar constriction which is enhanced by stimulation of the renin angiotensin system by potent diuretics leading to an accentuation of the renal effects of ACE inhibitors.

Absorption of intramuscular human recombinant tissue type plasminogen activator (rt-PA) facilitated by methylamine: potential applications for coronary thrombolysis

K A A Fox, A K Robison, R U Rodriguez, L E Fields, S S Sarnoff, B E Sobel
University of Wales College of Medicine, Cardiff; and Washington University, St Louis, Missouri, USA

Expedition administration of intramuscular (im) t-PA after infarction may maximise salvage of the myocardium with minimal systemic proteolysis. We have previously induced coronary thrombolysis with intracoronary or intravenous t-PA or with im t-PA by enhancement of absorption with hydroxylamine and electrical field stimulation. However, hydroxylamine induces transient haemodynamic effects and methaemoglobinaemia. In this study we characterised factors influencing im absorption of t-PA and the potential utility and toxicity of analogues of hydroxylamine (HA) in 109 rabbits. Absorption was measured after im injection of 1.5–13.0 mg/kg of rt-PA (50 mg/ml) in solution with HA (2.6–175 mg, n=25), in hypertonic media (0.63 mol/l sodium chloride, n=2), with vasodilators (0.01 mol/l adenosine or 0.09 mol/l hydralazine, n=5), with analogues of HA (n=72) or t-PA alone (n=5). Methylamine was particularly effective, lacked the haemodynamic effects associated with HA, and was not associated with methaemoglobin production. Methylamine plus field stimulation elicited functionally active blood levels of t-Pa within 5 minutes of injection that were of similar magnitude to those achieved with HA (200 vs 361 ng/ml for 1.5 mg t-PA/kg, n=12), with 20% blood activity remaining after 30 minutes. Only modest inflammation and interstitial haemorrhage were evident microscopically at the injection site after 48 hours. Vasodilators, hypertonic media, reduced amounts of HA or rt-PA alone led to much lower blood levels of rt-PA (14, 65, 46, 4 ng/ml/mg rt-PA respectively). Thus enhancement of absorption of t-PA with methylamine leads to dose dependent effective

(fibrinolytic) blood levels of rt-PA after im injection (200 to 954 ng/ml) without the potentially deleterious effects associated with other absorption enhancing agents.

Treatment of end stage heart failure by ultrafiltration

L Donato, A Biagini, C Contini, A l'Abbate, M Emdin, M Piacenti, R Palla
CNR Institute of Clinical Physiology, Institute of Medical Pathology, Haemodialysis Unit-2nd Medical Clinic, University of Pisa, Pisa, Italy

Seven patients (6 male; age range 36–73 yr) in end stage heart failure were treated by ultrafiltration of venous blood through a polyacrylonitrile membrane (1.1 m²; cutoff point MW 20 000). All patients were in class IV NYHA with primary congestive cardiomyopathy (2 cases) or ischaemic heart disease (5 cases); all had been treated with inotropic (I), diuretic (D), and vasodilator (V) agents in different combinations and had shown diminished response to drugs (despite increasing dosages), ingravescant oliguria, gain in body weight, and refractory oedema. One to five sessions of ultrafiltration were performed over a maximum of nine days with a body weight loss of 3.5 to 14.7 kg. Clinical improvement (respiratory distress and oedema) occurred rapidly; heart failure reappeared in one patient two weeks after ultrafiltration, and death followed in a few days; a second patient had a successful heart transplantation three weeks after ultrafiltration; in the remaining five treatment with I/D/V at moderate dosage was resumed after ultrafiltration and a pronounced clinical improvement (NYHA II/III) was maintained. One patient died a year later from stroke, and four are still alive 3, 6, 9, and 21 months after ultrafiltration treatment.

These data suggest that in end stage heart failure ultrafiltration may help in restoring the response to medical treatment and in improving clinical state in cases where heart transplantation is not immediately accessible or not indicated.

Neuroendocrine mechanisms in acute myocardial infarction

H M McAlpine, I N Findlay, G Gillan, Esther Henderson, J T Wilson, H J Dargie
Cardiac Department, Western Infirmary, Glasgow

In acute myocardial infarction inappropriate or excessive neuroendocrine activation may have important physiological consequences; little is known about the relation between the magnitude of such stimulation and the extent of myocardial dysfunction. We investigated the extent of activation of the renin-angiotensin system in 36 consecutive patients after myocardial infarction. Left ventricular ejection fraction (LVEF) was assessed by gated radionuclide ventriculography within 6 hours of the onset of symptoms and plasma active renin and catecholamines were measured on admission and again on day 3. Mean renin concentration was $70.4 \mu\text{U/ml}$ (range 4–549) on admission with similar concentrations in uncomplicated cases (group 1, $n=25$) and in heart failure (group 2, $n=11$; 73.4 (23) *vs* 63.7 (22) (SEM)). LVEF was lower in group 2 (23 *vs* 35%; $p<0.005$) in whom peak creatine kinase concentration were higher (3250 *vs* 2190 U/l; $p<0.05$). Renin concentrations were within the normal range ($10\text{--}50 \mu\text{U/ml}$) in 23/36 patients on admission compared with only 6/36 on day 3. Mean renin rose to 251 (115) $\mu\text{U/ml}$ but was significantly higher in group 2 than in group 1 (591 *vs* 103; $p<0.05$). Catecholamine concentrations were raised on admission—adrenaline 1.7 (0.6) nmol/l (normal range, undetectable–0.2), noradrenaline 3.6 (0.95) nmol/l (normal range 0.8–3.0), with higher concentrations in group 2 than in group 1 (3.68 *vs* 0.51 ($p<0.01$) and 6.35 *vs* 1.93 ($p<0.02$) respectively). By day 3, although catecholamine concentrations had fallen, noradrenaline concentrations remained significantly higher in the patients with heart failure—4.83 *vs* 1.62 nmol/l; ($p<0.001$). Thus significant activation of the renin-angiotensin and sympathetic nervous systems occurs in myocardial infarction, particularly in those with extensive infarcts leading to heart failure, but renin remains raised in many uncomplicated cases and this might not be wholly beneficial for tissue perfusion and myocardial function.

Changes in nuclear magnetic resonance during the first two weeks after myocardial infarction in man

M Been, M A Smith, J P Ridgway, J J K Best, D P de Bono, A L Muir
Royal Infirmary, Edinburgh

The magnetic resonance parameter t_1 (spin lattice relaxation time) of myocardium increases after coro-

nary occlusion of 30 min in dogs and increases further with occlusion of 2–3 hours. Changes are more pronounced if reperfusion is allowed. These changes correlate with myocardial water content. Our preliminary studies demonstrated increases in t_1 after myocardial infarction in man with values above 390 ms (normal 305 (25) ms). We now report t_1 changes during the 14 days after myocardial infarction, comparing patients with ($n=23$) and without ($n=11$) coronary reperfusion. Patients were imaged in a low field resistive imager (0.08 tesla) and t_1 maps were obtained for 16 mm transverse and coronal sections. For analysis the myocardium was divided into six standard regions of interest for each section. Thirty three of the 34 patients studied within two weeks of infarction had a t_1 value above 390 ms; at day 1–3 the maximum t_1 was 413 (29) ms ($n=23$) compared with 430 (41) ms ($n=22$) at day 4–7 and 436 (40) ms ($n=24$) at day 8–14. Four of the 23 patients studied at day 1–3 had normal t_1 values which subsequently became abnormal. The number of regions with an increased t_1 at each interval was 2.0 (1.5), 2.6 (2.4), and 2.8 (1.9) respectively. There was no significant difference between patients with or without reperfusion. The delayed increase in t_1 mirrors the reparative process and events other than oedema must also influence this relaxation parameter.

Placebo controlled investigation of anisoylated plasminogen streptokinase activator complex (APSAC) for thrombolysis in acute myocardial infarction

A D Timmis, B Griffin, J C P Crick, E Sowton
Guy's Hospital, London

Anisoylated plasminogen streptokinase activator complex (APSAC) is a new agent designed to produce thrombolysis without a major effect on systemic coagulation variables. This report describes the first placebo controlled double blind reperfusion study of APSAC in acute myocardial infarction. Unequivocal documentation of reperfusion was provided by coronary angiography before and after the drug intervention. Twenty patients with acute transmural infarction underwent coronary angiography 3.0 (1.1) hours after the onset of symptoms. This demonstrated total occlusion of the infarct vessel in 16 cases. The patients were then randomised to intravenous APSAC 30 mg ($n=9$, group A) or placebo ($n=7$, group B) 3.2 (1.1) hours after the onset of symptoms. Repeat angiography 90 minutes later

demonstrated reperfusion in six of group A but in none of group B ($p < 0.05$). Reperfusion was associated with an early peak in serum creatine kinase ($9.6(3.9)$ vs $21.7(4.7)$ hours) ($p < 0.05$). Full cardiac catheterisation was undertaken at three days to guide subsequent management. Persistent luminal patency was present in all but one of the six patients with early reperfusion and three additional patients showed late reperfusion (two group A, one group B). No haemorrhagic complications occurred during the study. One patient from group B died in intractable heart failure. These preliminary data confirm the thrombolytic efficacy of APSAC in acute myocardial infarction and indicate that the drug may be used safely by the intravenous route with a 66% early reperfusion rate.

Analysis of electrocardiographic changes occurring during thrombolytic therapy for acute myocardial infarction

S G Richardson, Patricia Morton, J G Murtagh, M E Scott, D B O'Keeffe
Cardiac Unit, Belfast City Hospital, Belfast

Electrocardiograms from 100 patients on thrombolytic treatment for coronary thrombosis were reviewed. Two groups were identified—52 patients (52%) showed abrupt reduction 60–120 minutes after treatment in both ST segment ($p < 0.01$) and T wave height ($p < 0.01$) with resolution of reciprocal changes. These changes did not occur in the remaining 48 patients (48%). Atrial fibrillation, ventricular extrasystoles, tachycardia, and fibrillation were evenly distributed throughout the two groups. Idioventricular rhythm occurred in 16 patients; 13 of these patients had simultaneous ST and T wave changes. At arteriography open infarct related arteries were found in 47 patients (94%) in the group with clear electrocardiographic changes and in 29 (60.4%) of those with no change. Open arteries were also present in 14 of 15 patients (93%) showing idioventricular rhythm. Two patients were excluded from analysis because of obvious clinical re-occlusion. A trend in ejection fraction was seen; values were highest in patients with clear electrocardiogram change (46.9%) and lowest in those with occluded arteries (42.2%).

After thrombolysis for infarction 52% of patients show clear abrupt change in ST elevation and T wave height. These changes were 79% specific and 63.5% sensitive for coronary re-opening as judged

by angiography. Idioventricular rhythm was a frequent and highly specific (96%) indicator of coronary re-opening; however, it was relatively insensitive (22%). A trend towards improved left ventricular function was seen in patients with clear abrupt electrocardiogram changes. Careful scrutiny of routine 12 lead electrocardiograms provides useful and accurate information relating to myocardial reperfusion after thrombolytic treatment.

Changes in left ventricular regional asynchrony after intracoronary thrombolysis

D G Gibson, H Mehmehl, F Schwarz, K Li, W Kübler
Brompton Hospital, London, and University Medical Clinic Heidelberg, West Germany

To study changes in asynchronous left ventricular wall motion after intracoronary thrombolysis, ventriculograms were obtained before and 4.3(2.5) weeks after lysis in 23 patients treated within 3.5(3.1) hours of the onset of pain. Lysis was achieved in 19, and patency was maintained at restudy in 16. Angiograms were digitised frame by frame, LV volumes, ejection fraction, and peak ejection rate were unchanged, and peak filling rate fell whether or not the artery was patent. Regional wall motion was studied by means of isometric and contour plots. The affected area showed simple hypokinesis in 10 patients, which was unchanged at restudy in nine and improved in one. Delayed inward motion during isovolumic relaxation was present in 14 cases, with or without additional hypokinesis; it improved in eight and returned to normal in six—more often than it did in simple hypokinesis ($p < 0.02$). Dyskinesis (three cases) and hyperkinesis (five cases) resolved in all. Outward motion during isovolumic relaxation reverted to normal in four of five cases, and outward motion reverted to normal during isovolumic contraction in five of seven. Improvement was more frequent when the affected artery was uncompromised by residual stenosis ($p < 0.01$). Arterial flow was re-established and maintained more often when the affected area showed asynchrony rather than simple hypokinesis ($p < 0.025$). Conclusions: (1) Asynchronous motion is the commonest regional abnormality early after coronary artery thrombosis. (2) Its increased frequency of recovery confirms that it represents residual contractile activity. (3) Its presence increases the chance of flow being re-established with lysis in the affected coronary artery.

Trial of early nifedipine treatment in patients with suspected myocardial infarction (the TRENT study)

R G Wilcox, J R Hampton, D C Banks, J Birkhead, I Brooksby, C Burns-Cox, M J Hayes, M Joy, A D Malcolm, H G Mather, J M Rowley
TRENT Co-ordinating Centre, Department of Medicine, University Hospital, Nottingham

Approximately 9000 consecutive patients admitted with suspected myocardial infarction to coronary care units (CCU) in nine hospitals were considered for admission to a randomised double blind study designed to compare the effect on mortality of nifedipine 10 mg four times a day with that of placebo treatment. 4700 patients were excluded but were nevertheless followed and their overall fatality rate at one month was 18%. 4488 patients were randomly allocated to nifedipine or placebo treatment which started immediately after assessment in the CCU, and the groups proved to be well matched. 64% of patients in both treatment groups sustained an acute myocardial infarction. 595 (26%) of the 2238 patients allocated to nifedipine treatment were withdrawn from the study as were 562 (25%) of the 2250 patients allocated to placebo treatment. All the patients were followed for one month, the duration of the study period. 150 (6.7%) of the patients initially allocated to nifedipine treatment died in the first month, compared with 141 (6.2%) of those initially allocated to placebo. The one month infarct mortality rates were 10.2% and 9.2% respectively. By "intention to treat" analysis there was thus an increase in overall mortality of 8% in the nifedipine group (95% confidence intervals +30% to -14%). Although this result embraces a small potential benefit from nifedipine treatment the trial was discontinued on the advice of the ethical committee who considered that it was unlikely that a statistically confident beneficial effect would be demonstrated if the trial were continued. Analysis of the subgroups formed when the results were available did not suggest that any group of patients with suspected myocardial infarction might benefit from early nifedipine treatment.

Impaired right ventricular function following transvenous fulguration of atrioventricular conduction

P M Schofield, R J Bowes, G Lawrence, M Prescott, N Brooks, D H Bennett

Regional Cardiac Centre, Wythenshawe Hospital, and Department of Nuclear Medicine, Manchester Royal Infirmary

After transvenous fulguration of atrioventricular (AV) conduction, 13 of 22 patients who had had no evidence of structural heart disease before the procedure complained of exertional dyspnoea. Patients were aged 19-63, 17 were female, and 16 had had AV re-entrant tachycardia. Resting right and left ventricular ejection fractions (RVEF and LVEF) were blindly measured by radionuclide angiography 10-42 months after fulguration. RVEF was significantly lower in patients who complained of exertional dyspnoea (33.8 (8.4)%, mean (SD), range 21-48%) than those who remained free of dyspnoea (40.5 (4.1)%, range 37-48%, $p < 0.05$) and also compared with a control group of eight subjects with no cardiorespiratory disease (41.9 (7.0)%, $p < 0.05$). There was no difference in LVEF between patients who complained of dyspnoea (52.5 (13.8)%) and those who did not (52.6 (5.0)%). Similarly, there was no difference in the number of shocks (1.9 (0.9) and 2.1 (0.6)) or total energy delivered (658 (291) J and 711 (198) J respectively) between the two groups. Exercise capacity (Bruce protocol) as a percentage of predicted normal value was significantly lower in patients who complained of dyspnoea (51 (24)% vs 81 (13)%, $p < 0.01$). We conclude that right ventricular function may be impaired in some patients after transvenous fulguration of AV conduction and that this may contribute to their reduced exercise capacity and exertional dyspnoea.

Three deaths after attempted high energy catheter ablation of ventricular tachycardia

D W Davies, A W Nathan, A J Camm
St Bartholomew's Hospital, London

Catheter ablation of ventricular tachycardia (VT) may abolish VT without the need for drugs or operation. However, the extent of the damage produced is unpredictable. Three cases of VT that illustrate potential problems of this treatment are described. All these patients were refractory to antiarrhythmic drugs and two were not suitable for surgical resection because of poor left ventricular (LV) function resulting from myocardial infarction (MI). The first patient had right ventricular (RV) dysplasia and VT originating from the RV outflow tract that was provoked only by strenuous exercise. After two attempts at catheter ablation with up to 400 J, the VT

on exercise was reduced to four beats. Two weeks later he suddenly became dyspnoeic and dizzy on mild exertion and died. The second patient had an LV aneurysm and incessant VT originating from the apical septum with earliest activation on the RV aspect. A transseptal shock of 200 J was unsuccessful so 360 J was delivered to the RV apical septum. The patient collapsed within minutes of this procedure. Cardiac tamponade was confirmed at necropsy without any discernible damage to the fibrotic LV septum. The third patient developed incessant fascicular tachycardia after a second MI. On four occasions, multiple DC shocks of up to 360 J were delivered both to the region of the posterior fascicle and the His bundle. Although it was initially suppressed, fascicular tachycardia returned and, after the last procedure, it was accompanied by paroxysmal ventricular flutter. Despite combination drug treatment the patient died suddenly two months later. Catheter ablation should be avoided at the RV apex, it may be ineffective on fibrotic endocardium, and can provoke malignant ventricular arrhythmias. It should be reserved for patients in whom other treatment is either ineffective or unsuitable.

Assessment of the haemodynamic consequences of varying pacemaker modality by Doppler ultrasound

I A Simpson, A B Houston, A C Rankin, A P Rae
University Department of Medical Cardiology,
Royal Infirmary, Glasgow

Doppler ultrasound was used to assess the haemodynamic consequences of varying pacing modalities in 10 patients during electrophysiological study. Cardiac output estimation, by a previously validated Doppler method, was made during atrial, ventricular, and atrioventricular sequential pacing at cycle lengths of 400 ms up to 800 ms. Atrioventricular intervals for sequential pacing ranged from 50 ms to 250 ms. Examination was performed with a Vingmed Alfred Doppler velocimeter with spectrum analysis and separate cross sectional echocardiographic imaging. Cardiac outputs were significantly lower during ventricular pacing (4.1 (1.5) l/min) compared with either atrial (5.1 (1.5) l/min, $p < 0.005$) or optimal atrioventricular sequential pacing (5.4 (1.6) l/min, $p < 0.001$). Varying the atrioventricular interval pro-

duced changes in cardiac output at each cycle length; these were more pronounced at shorter cycle lengths (mean change 12% at 700 ms and 21.5% at 400 ms, $p < 0.001$). The atrioventricular interval giving optimal cardiac output was unpredictable, varying with cycle length and between individuals. In conclusion, Doppler ultrasound can provide a simple non-invasive method of determining the haemodynamic consequences of intracardiac pacing, with the potential to predict the optimal pacing modality in individual patients before permanent pacemaker insertion.

Haemodynamic assessment of dual chamber pacing in hypertrophic cardiomyopathy using radionuclide ventriculography

J Erwin, E McWilliams, G Gearty, B Maurer
St Vincent's Hospital, Royal City of Dublin
Hospital, Dublin

To assess the mechanism of haemodynamic improvement in patients with hypertrophic cardiomyopathy in whom DDD pacemakers had been implanted because of failure of conventional medical treatment, six patients (mean age 47 years, range 22–48) were studied by gated radionuclide ventriculography in different modes of pacing. The patients were imaged in sinus rhythm (SR), VVI, and DDD modes with a three minute interval between each study. Measurements made were ejection fraction (EF), time to peak filling rate (TPFR), time to peak ejection rate (TPER), and percentage of stroke volume ejected during the first third of systole. Results showed no difference in EF between pacing modes. The TPFR was 574 (54) ms (mean (SD)) in SR, 571 (37) ms in VVI mode, and 524 (22) ms in DDD mode. The TPER was 169 (22) ms in SR, 209 (67) ms in VVI mode, and 193 (31) ms in DDD mode. The percentage of the stroke volume ejected during the first third of systole was 55 in SR, 40 in VVI mode, and 45 in DDD.

It is concluded that radionuclide ventriculography is a useful non-invasive method for following the progress of these patients; normalisation of left ventricular filling and ejection occurs with DDD pacing in hypertrophic cardiomyopathy; the mechanism of improvement is probably asynchronous left ventricular contraction with appropriately timed atrial synchrony.

An intra-patient comparison of ambulatory blood pressure during chronic DDD and VVI pacing

N A Boon, A J Frew, S M Cobbe
John Radcliffe Hospital, Headington, Oxford

Fifteen patients (age 54–81 years) with programmable dual chamber pacemakers (Cordis 233F or Biotronik Diplos 05) were randomly allocated single blind to DDD or VVI pacing. After an equilibration period of at least four weeks each patient underwent an assessment of symptoms by visual analogue scales and a 24 hour intra-arterial ambulatory blood pressure recording. The pacemaker was then programmed to the opposite mode and the observations were repeated after another period of at least four weeks. 12 of the 15 patients expressed a strong symptomatic preference for DDD pacing; patients also reported significantly more dyspnoea, fatigue, and dizziness during VVI pacing (in each case $p \leq 0.05$, Wilcoxon rank sign test). Computer aided beat by beat analysis showed that blood pressure was significantly lower and significantly more variable during VVI pacing. The mean (SEM) daytime systolic blood pressure was 139.3 (3.8) mmHg during DDD pacing compared with 131.3 (4.5) mmHg during VVI pacing ($p < 0.05$, paired t test). The median (range) standard deviation of daytime systolic blood pressure, an index of blood pressure variability, was 18.5 (15–28) mmHg during DDD pacing and 24 (14–31) mmHg during VVI pacing ($p < 0.005$, Wilcoxon rank sign test). Hence, transient episodes of hypotension were more common during VVI pacing, which may partly explain why the patients in general felt better during DDD pacing.

Activity sensing rate responsive permanent cardiac pacing in very young children

E J Ladusans, O Jones, M Tynan, P V L Curry
Guy's Hospital, London

Single chamber ventricular pacemakers which can vary the pacing rate according to sensed physical activity should be especially advantageous in very young children in whom dual chamber physiological pacing is often technically difficult to achieve. Five young children mean age 5.8 years (range 3.3–11) and a two week old infant have received small single chamber activity sensing rate responsive pacemakers

(Medtronic Activitrac). The indication for pacing was complete heart block in all cases (four had associated structural heart disease). Pacemakers were implanted in the abdomen in five children and in the pre-pectoral region in one. Five patients had endocardial electrodes (including the neonate) and one child had an epicardial lead. In five children effort capacity could be determined by treadmill exercise tests (Bruce protocol). Duration of exercise was prolonged by an average of 1.7 (0.1) minutes (SEM) in the rate responsive mode compared with fixed rate demand pacing (VVI) between 70 and 90 beats/min, the standby VVI rate being predetermined by programming and using the spontaneous atrial rate as a guide. In the two week old baby the pacemaker was programmed to give maximum heart rate response with the lowest activity threshold. Holter monitoring showed an average ventricular rate of 110 beats/min with a maximum of 140 beats/min. We conclude that even in very small children rate variable pacing in response to physical activity is feasible and permits more physiological heart rate responses.

The effect of right and left ventricular function on early and late mortality following surgical repair of post-infarction ventricular septal defect

P M Schofield, M Jones, R A M Lawson,
A K Deiraniya, C Ward, C L Bray
Regional Cardiac Centre, Wythenshawe Hospital,
Manchester

Preoperative investigations of 60 patients (aged 46–73) who underwent repair of post-infarction ventricular septal defect (VSD) were reviewed to assess the effect of right and left ventricular function on early (< 30 days) and late mortality. Left ventricular ejection fraction (LVEF) was calculated from right anterior oblique ventriculograms; right ventricular (RV) function was assessed by measuring per cent reduction in RV mid-cavity diameter from left anterior oblique ventriculograms. There were 23 early deaths and these patients had a significantly lower per cent reduction in RV mid-cavity diameter (16.5 (9.5)%, mean (SD)) than the 37 survivors (26.7 (10.6)%, $p < 0.01$). There was no difference in LVEF (33.8 (10.2)% and 31.7 (9.7)% respectively) between the two groups. The 37 survivors have been followed up for 2–108 (mean 38) months and there have been 14 late deaths. There was no difference in per cent reduction in RV mid-cavity diameter

between those who died (26.0 (12.2)%) and those who survived (27.1 (9.8)%), but LVEF was significantly higher in the survivors (26.2 (9.3)% *vs* 35.0 (8.5)%, $p < 0.01$). Early mortality was associated with inferior rather than anterior infarction ($p < 0.01$), but the late result was not related to infarct site. We conclude that after surgical repair of post-infarction VSD, site of infarction and right ventricular function are major determinants of early mortality, whereas left ventricular function is more important in determining the long term prognosis.

Ventricular function following heterotopic cardiac transplantation

A G Mitchell, M H Yacoub
Harefield Hospital, Harefield, Middlesex

Ventricular function has been studied in 16 patients one year after heterotopic cardiac transplantation and in 11 of these after a second year. This group is taken from 26 patients undergoing heterotopic cardiac transplantation from January 1983. Five died early and five have not reached the first anniversary. Heterotopic cardiac transplantation was combined with aneurysmectomy in 11 and with coronary artery bypass graft in 12. One underwent donor excision for rejection after one year. All survivors have good exercise tolerance achieving 9.7 (3.1) min and 8.7 (3.2) min of the Bruce exercise protocol at one and two years. Diastolic pressures were lower in the donor heart with left ventricular end diastolic pressure being 11.7 (6.1) mm Hg in the donor and 14.2 (4.9) mm Hg in the recipient. Mean pulmonary capillary wedge pressure was 12.4 (4.6) mm Hg and mean mitral valve gradient was higher for the donor hearts. Systolic function was better in the donor heart with higher peak systolic pressure (143 (17.6) mm Hg) than the recipient (120 (26.6) mm Hg) and a faster rise of pressure. Peak systolic pressure was frequently augmented when the ventricles contracted together. Left ventricular angiography showed very good donor function in 14 at one year and nine at two years. Five patients with aneurysm resection showed good ejection from recipient ventricle to aorta, all with ejection fraction over 30%. One other had good ejection and four modest ejection from the recipient ventricle. Clot was present in seven recipient ventricles. Cardiac performance after heterotopic cardiac transplantation remains good for two years and a proportion retain significant recipient function.

Medial and endothelial damage can be avoided during surgical preparation of autologous saphenous vein coronary bypass grafts

G D Angelini, A C Newby, H M J Williams,
N Kulatilake, S Passani, I M Breckenridge
University Hospital of Wales, Heath Park, Cardiff

Damage to saphenous vein media and endothelium during surgical preparation may promote subsequent coronary vein graft occlusion. ATP concentration and ATP:ADP ratio were measured to assess medial function and stimulated (vortex mixing) prostacyclin production to assess endothelial function. Freshly isolated vein had 450 (20) nmol/ATP/g, an ATP:ADP ratio of 2.4 (0.1) ($n = 38$), and produced prostacyclin at 13 (1) nmol/g ($n = 52$). Vein subjected to conventional surgical preparation (dissection, adventitial stripping, side branch ligation, distension at < 300 mm Hg and per-operative storage in patient's heparinised arterial blood at 23°C, distal anastomosis following cardioplegic arrest, and subsequent proximal anastomosis) had an ATP concentration of 260 (40) nmol/g, an ATP:ADP ratio of 1.3 (0.1) ($n = 16$), and produced prostacyclin at 6.3 (0.9) ng/min per g ($n = 14$) ($p < 0.001$ *vs* freshly isolated vein for all three variables). Vein subjected to a modified procedure (side branch ligation followed by anastomosis to the ascending aorta using an exclusion clamp, distension at arterial pressure after temporary removal of the clamp, and distal anastomosis during subsequent cardiopulmonary bypass/cardioplegic arrest) had an ATP concentration of 480 (80) nmol/g, an ATP:ADP ratio of 2.5 (0.1) ($n = 8$), and produced prostacyclin at 12 (2) nmol/min g ($n = 11$) (NS *vs* freshly isolated vein, $p < 0.001$ *vs* conventional preparation for all three variables).

Thus conventional surgical preparation damages both the venous media and endothelium. Damage can be avoided, however, with the modified procedure. The impact of improved intraoperative preservation on graft patency may now be tested.

Ten years' clinical experience with the pericardial xenograft

M I Ionescu, A P Tandon, M Chidambaram,
N P Silverton
Royal Halifax Infirmary and Leeds General Infirmary

Since 1975, 1018 pericardial valves have been implanted in 741 patients. Single valve replacement was undertaken in 224 patients with aortic (AV), 302 patients with mitral (MV), five patients with tricuspid valve disease, and 190 patients had multiple valve (DV) replacement. Of the total number of valves used 578 were standard and 440 low profile Ionescu-Shiley pericardial xenografts. Hospital mortality was 6.3%. The 714 hospital survivors were followed up for 3 to 111 (mean 51.9) months. Long term anticoagulants were not used. The predicted actuarial survival rates are 85.8(8.7)% for AV, 84.1(7.8)% for MV, and 80.2(10.3)% for DV 10 years after operation. Valve thrombosis was not observed. The actuarial freedom from embolism was 96.4(2.7)% for AV, 96.8(2.3)% for MV, and 97.2(2.0)% for DV at 10 years after valve replacement; the linearised incidence being 0.55 episodes per cent per annum for AV, 0.62 for DV, and 0.55 for MV. Twenty five pericardial xenografts were replaced because of dysfunction (valve abrasion and calcification were responsible for 16 and 8 valve failures respectively). The linearised incidence of valve dysfunction was 0.77 episodes per cent per annum; the actuarial predicted freedom from valve dysfunction being 83.0(9.1)% for AV, 89.3(7.0)% for MV, and 82.4(11.0)% for DV 10 years after operation. The valve durability was 87.8(4.9)% for standard pericardial xenografts at 10 years and 99.4(0.6)% for low profile pericardial xenografts at 5 years after valve replacement.

These clinical experiences confirm the long term durability of the standard pericardial xenograft and the in vitro superiority of the low profile pericardial xenograft.

Can left ventricular ejection fraction by cine computed tomography be determined by a single slice?

M R Rees, R M Macmillan, V Maranhao, D L Clark Killingbeck Hospital, Leeds; and Deborah Heart and Lung Center, New Jersey, USA

Cine computed tomography is a new cardiac imaging technique. Non-gated images can be obtained at 17 frames/second. 27 patients were divided into two groups. Group 1 (10 females, 5 males, age 35–74) underwent cine CT in the transaxial view (no rotation no tilt). Group 2 (3 females, 9 males, age 46–70) had cine CT in the long axis view (20°C counter-clockwise angulation, no tilt). Contrast was injected

via an antecubital vein and timed for maximal opacification of the ventricles. The left ventricle (LV) was imaged in the movie mode in contiguous slices of 8mm thickness. End systolic and end diastolic frames were identified for each slice. LV cavity areas were determined by two methods (M_1 or M_2) of edge detection (M_1 =unassisted visual; M_2 =setting of the Hounsfield level at half the difference between the contrast in the cavity and the myocardium with the window width at one). LVEF was measured by summation of end diastolic (EDV) and end systolic (ESV) values for each slice and by selecting the largest central slice by volume for ESV and EDV. LVEF as an average of two sinus beats was measured in all patients by right anterior oblique single plane contrast ventriculography at catheterisation using the area-length method. In group 1 there was poor correlation between catheter EF and cine/CT midslice EF (M_1 , $r=0.69$, M_2 , $r=0.76$) and total volume EF (M_1 , $r=0.77$; M_2 , $r=0.81$). For group 2 there was good correlation between catheter EF and cine/CT midslice EF (M_1 , $r=0.96$; M_2 , $r=0.93$) and total volume EF (M_1 , $r=0.96$; M_2 , $r=0.93$). It is concluded that the view used affects the accuracy of the examination, that edge detection plays a less important role than cardiac orientation, and that a single slice in the long axis view can be used to calculate ejection fraction.

The clinical value of a new myocardial imaging agent—technetium-99m tertiary butyl isonitrile (Tc-99m BIN)

M N Khalil, J R Thornback, K M Patel, M Y Early, G Hartley, D N Taylor, J M Berry, P J B Hubner Cardiology Department, Groby Road Hospital, Leicester

Technetium-99m is less expensive and has a more favourable energy emission for scanning with a gamma camera than thallium-201. A new myocardial imaging agent, Tc-99m BIN, was studied in 50 subjects. There were five normal controls, 15 patients with myocardial infarction (MI), and 30 with angina due to angiographically documented coronary artery disease (CAD). After the intravenous injection of between 3 to 5 mCi of Tc-99m BIN, subjects were scanned by means of a gamma camera with a converging collimator. In normal subjects the myocardium was clearly seen at 60 minutes at rest and at 30 minutes when the subject was first exercised. Patients with MI were scanned at rest and defects in

myocardial uptake were clearly shown. Each patient with angina received thallium-201 and Tc-99m BIN separately after maximal treadmill exercise. Optimal images with Tc-99m BIN were obtained at 30 minutes after exercise and at four hours for redistribution scans. Reversible perfusion defects were seen and the images with Tc-99m BIN were superior to those obtained with thallium-201 in the same patients.

These studies suggest that Tc-99m BIN is a good myocardial scanning agent that may be superior to thallium-201.

An objective non-invasive method for detecting early diastolic dysfunction in patients with coronary artery disease

R Rodrigues, A Lahiri, E B Raftery
Northwick Park Hospital and Clinical Research Centre, Harrow

The demonstration of abnormal left ventricular (LV) diastolic function in ischaemic heart disease (IHD) has led to renewed interest in methods of assessing LV function non-invasively. An automated method for assessing LV diastolic function from equilibrium radionuclide angiography with Tc-99m has been developed. This technique was used to study 30 normal subjects and 39 patients with IHD. ECG gating was used to collect the data in 32 frames per cardiac cycle with 5% gate tolerance. A second derivative method of edge detection was used to define the LV in all frames. A high resolution time-activity curve was then obtained from which a first derivative sample was generated to identify points of peak filling and emptying. Peak filling rate (PFR, EDV/s), time to peak filling rate (TPFR, ms), filling fraction (FF), and early filling rate (EFR) (EDV/s) were calculated. The mean (SEM) normal values were: PFR 3.1 (0.07), TPFR 168 (8), FF 0.52 (0.03), EFR 1.5 (0.7). These were all significantly different in the patients: PFR 2.0 (0.08), TPFR 197 (9), FF 0.31 (0.2), EFR 1.0 (0.06) ($p < 0.001$, $p < 0.05$, $p < 0.001$, and $p < 0.001$ respectively). This study confirms that diastolic function is abnormal in IHD and that this may be detected before systolic dysfunction becomes apparent. This automated technique may be used to give a reliable objective assessment of diastolic function and to follow patient response to therapeutic interventions.

A new non-invasive method of estimating left ventricular end diastolic pressure using pulsed Doppler ultrasound

K S Channer, W Culling, P Wilde, J V Jones
Cardiology Department, Bristol Royal Infirmary, Bristol

Left ventricular end diastolic pressure (LVEDP) is generally regarded as a useful indicator of left ventricular function. Its measurement has previously relied on invasive techniques. A new non-invasive method of estimating LVEDP is described. We have compared the ratio of the passive and active components of mitral flow with LVEDP measured at cardiac catheterisation in 20 patients (14 males, mean age 51.9 years, range 36–62) with ischaemic heart disease. None had valve disease and all were in sinus rhythm. Pulsed Doppler measurement of mitral flow were performed using the apical view to position the sample volume in the mitral orifice, with simultaneous ECG and LVEDP recordings. Each spectrally analysed mitral flow trace showed two diastolic peaks. The first represented passive flow from left atrium to ventricle and the second represented active flow due to atrial contraction. The mean of 10 consecutive recordings of the ratio of the areas of the two wave forms was calculated for each patient and found to correlate with LVEDP ($r = 0.78$ $p < 0.001$). Active mitral flow was lower with higher LVEDP. Mitral flow ratios of > 2 were always associated with LVEDP > 20 mm Hg. Reproducibility of the mitral flow ratio was assessed by making 10 separate measurements on the same individual within one hour; the correlation coefficient was 7.2%.

In conclusion, this technique offers a non-invasive and reproducible method of assessing LVEDP.

Single vessel angioplasty in multiple vessel disease

N P Silverton, N C Jackson, G I C Nelson
Department of Cardiovascular Studies, University of Leeds

To assess the safety and efficacy of single vessel angioplasty in multiple vessel disease (MVD), a retrospective assessment was made of the results in 115 patients who were treated by single vessel angioplasty before the introduction of multiple vessel angioplasty. According to the Coronary Artery Surgery Study criteria 90 patients (68 male and 22

female) had single vessel disease (SVD) and 25 patients (22 male and three female) had MVD with one artery suitable for mechanical treatment. Other diseased arteries were unsuitable for surgery because of inaccessibility or calibre (nine patients), diffuse disease (seven patients), or total occlusion with Q wave infarction in the dependent territory (nine patients). The vessels treated in patients with SVD were the left anterior descending (77), right coronary artery (9), and left circumflex (4); and in patients with MVD they were the left anterior descending (15), right coronary artery (7), and left circumflex (3). Short and long term follow up was conducted. Technical success was achieved in 71 of 90 patients with SVD and in 19 of 25 with MVD. Emergency bypass grafting was necessary in six patients with SVD and in one with MVD. One patient with MVD died within 24 h of angioplasty. Angina was totally abolished in 67 and improved in three of the 71 SVD patients with successful angioplasty and was abolished in 13 and improved in four of 19 MVD patients who had successful angioplasty. In this small group of patients with MVD who had only one artery suitable for mechanical treatment, angioplasty was acceptably safe and improved symptoms. Thus single vessel angioplasty may have a place in the treatment of patients with multiple vessel coronary artery disease.

Evolution of myocardial ischaemia during percutaneous transluminal coronary angioplasty

B Griffin, J C P Crick, A D Timmis, E Sowton
Guy's Hospital, London

Balloon inflation during coronary angioplasty is a useful model of acute coronary occlusion and regional myocardial ischaemia. The prevalence and duration of ischaemia during successive 60 second balloon inflations were assessed in 16 patients (11 with left anterior descending artery and five with right coronary artery lesions) by continuous six lead ECG and cross sectional echocardiography recording. ST segment elevation developed in 14 of the patients within 18(12) (SD) seconds of balloon inflation and returned to baseline within 20(9) seconds of deflation. Wall motion abnormalities on the echocardiogram were seen in all patients 15(5) seconds after balloon inflation and had disappeared 13(3) seconds after deflation. Time to onset of ischaemia as determined by both methods remained remarkably constant during successive balloon

inflations. The rate pressure product (RPP) before balloon inflation correlated inversely with time to onset of ischaemia detected by both techniques: $r = -0.72$, $p < 0.05$ (ECG); $r = -0.67$, $p < 0.05$ (echocardiography). Nevertheless, evidence of ischaemia developed within 30 seconds in all patients regardless of RPP. This investigation of regional ischaemia during percutaneous transluminal coronary angioplasty indicates that ECG and echocardiography have a similar sensitivity for detection of acute ischaemia; resting myocardial oxygen consumption as reflected by RPP is an important determinant of the time to onset of ischaemia; manipulation of RPP alone is unlikely to have an important protective effect during percutaneous transluminal coronary angioplasty.

Percutaneous laser thermal angioplasty

D C Cumberland, T A Sanborn, D I Tayler,
C L Welsh, A Greenfield, J Guben
Northern General Hospital, Sheffield; and Boston
University Medical Center, Boston, USA

The potential of laser energy in percutaneous angioplasty will not be realised until an intraluminal channel can be produced and vessel wall perforation can be reliably avoided. A metal tipped laser fibre (laser probe) with up to 10 W argon laser power was used for five to 60 s in 46 limbs in 44 patients undergoing percutaneous femoral/popliteal angioplasty. All 14 stenoses were successfully traversed. Of 32 occlusions (length 1 to 35 cm, mean 8 cm) 22 were initially probed at their proximal limits by a guide wire so that they could be classified as being potentially easy or difficult to cross by conventional means. Ten occlusions were classified as "impossible" because either previous attempts on angioplasty had failed or because they were anatomically unsuitable for conventional techniques. The probe successfully traversed all 10 easy, 11 of 12 difficult, and seven of 10 impossible occlusions. In one case mechanical wall entry with extravasation occurred (before laser energy was used) (this was probably due to a false passage produced by previous guide wire); there were no sequelae. In all the lesions that were successfully crossed an adequate initial channel (mean lumen diameter (MLD) 1.41 mm (0.27) (SD)) was produced for subsequent balloon dilatation (MLD 2.84 mm (0.88)).

Thus the laser probe facilitates angioplasty by providing an initial channel through lesions before

balloon dilatation. It can traverse occlusions that are difficult or impossible to cross by conventional means and therefore has potential for increasing the role of angioplasty in the treatment of arterial disease.

Percutaneous transluminal valvotomy for rheumatic mitral stenosis using a double balloon technique

M Al Zaibag, P Ribeiro, S Al Kasab
Riyadh Military Hospital (Adult Cardiology Division), Riyadh, Kingdom of Saudi Arabia

Severe mitral stenosis currently requires surgical intervention. The feasibility of mitral balloon valvotomy (that is commissural splitting) was demonstrated during cardiac surgery. A transatrial double balloon technique was then used to perform percutaneous mitral valvotomy in nine patients with rheumatic mitral stenosis. Nine symptomatic patients (23(6) years mean (SD) with severe non-calcific mitral stenosis who were in sinus rhythm were selected. The study protocol included left and right cardiac catheterisation, calculation of the mitral valve area by the Gorlin formula, and left atrial and left ventricular angiograms before and immediately after balloon dilatation. The left atrium was entered with two number 12 French Mullins transseptal sheaths from both femoral veins. Two pre-shaped 0.038 inch guide wires were positioned in the left ventricle, and two Medi-tech balloons (12 to 15 mm in diameter) were advanced across the mitral valve and simultaneously inflated up to 5 atmospheres. In seven patients, the mitral valve area increased from 0.71 (0.19) to 2.0 (0.8) cm², and the mean mitral gradient decreased from 15 (3.5) to 2.6 (2.7) mm Hg. The procedure was unsuccessful in the first two cases, in which small balloons (12 mm) were used. During inflation, systolic aortic pressure was maintained above 45 mm Hg. Three patients had trivial mitral incompetence after successful dilatation; otherwise there were no complications. No left to right shunt at the atrial level was detected by oximetry.

It is concluded that in selected patients severe rheumatic mitral stenosis can be successfully relieved by a percutaneous double balloon technique without complications.

Somatostatin: a neuroregulatory peptide with electrophysiological activity

S C Webb, W G Hendry, S R Bloom, D M Krikler
Royal Postgraduate Medical School, London

The peptide somatostatin, which acts in part as an automatic neurotransmitter, is present in human cardiac tissue, with high concentrations in the sinus and atrioventricular (AV) nodes. To assess the possible physiological and pharmacological roles of somatostatin in the heart, its electrophysiological effects were compared with those of the calcium antagonist verapamil in 10 patients undergoing investigation of AV re-entry tachycardia (accessory AV pathway 4; dual intranodal pathways, 6). During sinus rhythm, somatostatin (12.5 µg/min for 10 min) prolonged cycle length by 45 (37) ms (mean(SEM)) whereas verapamil shortened it by 30 (21) ms ($p < 0.01$). Somatostatin had a less pronounced effect than verapamil on AV nodal conduction as judged by prolongation of both AH interval (11 (3) vs 43 (8) ms, $p < 0.005$) and AV nodal effective refractory period (39 (8) vs 94 (38) ms, NS). Both drugs terminated tachycardia in 6/7 patients; verapamil after 35 (3) s by AV conduction block. With somatostatin, termination occurred later (after 277 (90) s); in 5/6 by invasion of the re-entry circuit by ventricular extrasystoles. Prolongation of tachycardia cycle length before termination was more pronounced with verapamil than with somatostatin (94 (19) vs 29 (11) ms, $p < 0.05$). The electrophysiological properties as well as the anatomical distribution of somatostatin suggest that it may participate in the mediation of autonomic control of the sinus and AV nodes.

The misdiagnosis of ventricular tachycardia—results of a postal survey

A W Nathan, J E Elstob, A J Camm
St Bartholomew's Hospital, London

Ventricular tachycardia may be misdiagnosed, and this can lead to serious consequences. A postal survey was carried out to examine the diagnostic accuracy of clinicians faced with this arrhythmia. Copies of referral ECGs from six patients with ventricular tachycardia who had been misdiagnosed as having supraventricular tachycardia were sent to a random selection of physicians. Each 12 lead ECG had ample data by classic criteria for the correct diagnosis to be made, and each patient also had an electro-

physiological study performed to optimise treatment and to confirm the diagnosis. The ECGs all showed a regular rhythm, and the rates ranged from 176 to 200 beats/min. Five had a QRS width ≥ 150 ms, five had a QRS axis $\geq 60^\circ$, five had atrioventricular dissociation, one had fusion beats, one had concordance across the chest leads, and three had morphological features that excluded bundle branch aberration.

There were 200 replies, 148 from consultants, 49 from those in training, and three from others. Fifty eight were cardiologists, 90 had a major cardiac interest, and 52 had other specialist interests. Twenty two were aged ≤ 30 , 79 were 31–40, 51 were 41–50, and 48 were ≥ 51 years. The diagnosis was correct in 558 (47%) of cases (ranging from 30–79% between ECGs). Twelve (6%) respondents had no correct answers, 46 (23%) had one, 41 (21%) had two, 38 (19%) had three, 21 (10%) had four, 20 (10%) had five, and only 22 (11%) had all replies correct. Forty two physicians (21%) had five or six correct answers including 20% of consultants and 27% of those training. This was also the result for 34% of the cardiologists, 22% of those with a major cardiac interest, and 4% of the others; and 26% of those aged 31–50 and 11% of the others.

Misdiagnosis of ventricular tachycardia was common despite characteristic ECGs and was made even by experienced cardiologists.

Drug related arrhythmia induction during electrophysiological testing

A P Rae, A M Greenspan, H R Kay, L N Horowitz
University Department of Cardiology, Royal Infirmary, Glasgow; and Likoff Cardiovascular Institute, Philadelphia, USA

Electrophysiological testing (EPS) has been suggested as a means of identifying the arrhythmogenic potential of antiarrhythmic drugs. The incidence of arrhythmia induction (AI) was determined in 314 patients with inducible ventricular arrhythmias undergoing 801 individual drug studies. The definitions of AI that were used and their incidence were (a) conversion of non-sustained ventricular tachycardia (VT) to a sustained arrhythmia (18%); (b) conversion of stable sustained VT to a sustained arrhythmia requiring cardioversion (7%); (c) reduction in aggressiveness of stimulation mode (20%); and (d) development of spontaneous sustained VT (0.5%). The drug regimens included 15 single

agents and eight combinations. The incidence of AI ranged from 15% to 37% (mean 23%) for single agents and from 22 to 30% (mean 29%) for combination regimens. Quinidine with the lowest incidence caused significantly less AI than amiodarone, flecainide, indecainide, quinidine plus mexiletine, and amiodarone plus procainamide ($p < 0.05$). No combination regimen caused significantly more AI than any other combination. In 40 studies of combination regimens, one component of which had previously produced AI, 22 (55%) did not manifest AI. Drug concentrations for single agents were all within the therapeutic range. In conclusion, drug-related AI is common during EPS and the development of AI while the patient is on a single agent does not preclude its use in combination regimens.

Indirect evidence for participation of His Purkinje system in ventricular activation during ventricular tachycardia

M Shenasa, M A Sadr-Ameli, M Fromer,
G Faugère, R Nadeau
Hôpital du Sacré-Coeur, University of Montreal, Canada

Currently there is not enough evidence to determine whether the His Purkinje system (HPS) participates in myocardial activation during ventricular tachycardia (VT). To test whether the HPS was engaged in ventricular activation during ventricular tachycardia the following were analysed (a) the effect during sinus rhythm of HPS conduction delay manifested as bundle branch block and (b) the effect of HPS conduction time (H-V interval) on the QRS duration of VT in 125 patients with sustained tachycardia. During sinus rhythm 67 patients had a narrow QRS complex and they all had normal H-V interval (mean 45.7 (5) ms), 34 patients had right bundle branch block with mean H-V interval of 49 (7) ms (NS compared with the former patients), and the remaining 24 patients had left bundle branch block and corresponding H-V interval of 63 (9) ms ($p < 0.05$ compared with those with narrow QRS). During VT, QRS duration of patients with narrow QRS ranged from 160 to 190 ms (mean 175 (12)) and in those with right and left bundle branch block it ranged from 190 to 240 ms (mean 205 (11)) and from 210 to 240 ms (230 (15)) respectively ($p < 0.05$ and $p < 0.02$ compared with those with narrow QRS). It is concluded that VTs in patients with left bundle

branch block during sinus rhythm and prolonged H-V interval have a longer QRS duration than those with narrow QRS and right bundle branch block. Thus, the presence of His Purkinje system conduction delay during VT may suggest its participation in ventricular activation during tachycardia.

Isosorbide mononitrate by intravenous bolus administration in acute left ventricular failure

M D Gammage, R G Murray, W A Littler
Department of Cardiovascular Medicine, University of Birmingham; and East Birmingham Hospital, Birmingham

Nitrates represent a therapeutic alternative to intravenous diuretics in the treatment of acute left ventricular failure, but isosorbide dinitrate is less convenient than diuretics as it must be given by infusion rather than bolus injection. Eleven patients with acute left ventricular failure after acute myocardial infarction were entered into an open haemodynamic study of isosorbide-5-mononitrate. All patients had clinical and radiographic evidence of left ventricular failure, confirmed by pulmonary capillary wedge pressure (PCW) > 20 mm Hg after insertion of a flow directed, thermodilution catheter into the pulmonary artery. After acquisition of baseline data, three bolus doses (5 mg) of isosorbide-5-mononitrate were given intravenously at 15 minute intervals. Mean PCW fell from 26.2 (6.8) mm Hg at control to 17.5 (8.5) mm Hg at 45 minutes ($p < 0.01$). Cardiac index fell from 2.4 (0.8) l/min-m² to 2.31/min/m² ($p < 0.05$) due to a fall in heart rate (103 (11) beats/min to 97 (15) beats/min, $p < 0.05$) as blood pressure, stroke volume index, stroke work index, and systemic vascular resistance were unchanged. All patients also experienced rapid symptomatic relief. These data suggest that isosorbide-5-mononitrate is a safe, convenient, and effective treatment for acute left ventricular failure when given by intravenous bolus injection.

Planned day case Sones's technique cardiac catheterisation

N H Murray, M T Rothman
Department of Cardiology, London Chest Hospital

Day case cardiac catheterisation was planned in 51% (855) of 1662 patients admitted during an 11 month period up to the end of 1985. Of these, 810 (95%) underwent uneventful cardiac catheterisation with brachial arteriotomy using the Sones's technique and were discharged the same day. All patients underwent coronary angiography with or without other catheter studies. Forty five patients (5%) were required to stay in hospital; in 18 (2%) the femoral route was used in addition, nine (1%) patients had severe angina with ST changes during the procedure, five patients (0.5%) were found to have important left main stem stenosis and were kept for elective bypass operation, two (0.12%) became hypotensive but were allowed home the following day, two remained in hospital because of oozing from the brachial arteriotomy, and two could not be discharged the same day for administrative reasons. There were no infarcts or deaths. Six patients had developed new medical problems since their pre-admission assessment such that they could be not catheterised as day cases. The remaining patients were unsuitable for day case investigation because of instability, requirement for femoral approach, or other medical or geographical reasons.

Day case cardiac catheterisation improves cost efficiency and can be achieved without compromising the safety of the patient or the diagnostic sensitivity.

Left bundle branch block: prevalence, incidence, follow up echocardiography, and exercise testing

G J Eliasson, K Pálsson, K Eyjólfsson, A Árnason, T Hardarson, N Sigfússon
Landspítalinn, University Hospital, Reykjavik, Iceland (Icelandic Heart Association)

In a screening study of a randomly selected population of 8450 men aged 33 to 61 and 9000 women aged 34 to 61 conducted in Iceland in 1967-1977, 27 men and 17 women were found to have left bundle branch block (LBBB). In 1977 the prevalence was 0.43% in men (mean age with LBBB 58.9 years) and 0.28% in women (mean age 58.5 years). The annual incidence of LBBB was 3.2×10^{-4} in men and 3.7×10^{-4} in women. All 36 surviving patients with LBBB were examined in 1984 by chest x ray, echocardiography, and exercise testing (Bruce protocol). Eight men and no women had had myocardial infarction ($p < 0.05$), nine men and three women had

angina pectoris, 10 women and five men had hypertension ($p < 0.02$, five men had cardiomyopathy, seven men and six women had primary conductive disease, two patients had complete atrioventricular block, four patients had had syncope, and three patients had pacemakers. Eleven patients were symptom free and 11 had mild and 14 had severe functional limitations. Five men and two women had died compared with 18 men and one woman in an age matched control group of 176 people (NS). Three of the five men with LBBB who died had cardiomyopathy at necropsy. Three men died suddenly. The two women died of non-cardiac causes. Only one patient in the control group had cardiomyopathy ($p < 0.01$). There was no significant difference in the distribution of other cardiac diagnoses between the groups. Eleven LBBB women out of 13 had an exercise test of normal duration (≥ 6 min) and 11/17 men exercised normally (≥ 7 min). Nine men and two women had an increased left ventricular diameter and three men and two women had a septal thickness of ≥ 1.5 cm by echocardiography. In comparison with the control group the LBBB patients had an increased left ventricular diameter $2.85 (0.38)$ vs $2.58 (0.38)$ cm/ m^2 body surface area ($p < 0.01$) and a non-significant increase in interventricular septal thickness. There was no difference in left atrial diameter between the groups.

In conclusion, cardiomyopathy in men and hypertension in women is associated with LBBB. The prognosis of LBBB is good and few patients require pacemakers. The left ventricular diameter was increased in a randomly selected group of patients with LBBB.

The relevance of coronary collateral flow in preserving left ventricular function

Ann Tweddel, W Martin, I McGhie, I Hutton
University Department of Medical Cardiology,
Royal Infirmary, Glasgow

The impact of collateral circulation of left ventricular function in response to physiological stress was determined in 50 patients at coronary angiography. Regional myocardial nutrient flow was obtained from the washout of xenon-133 at rest and immediately after maximal exercise. Fifty five collateral distributions were identified in 41 patients with coronary artery disease, of which 25 were seen angiographically and 30 by xenon-133 alone. Nutri-

ent flow increased in response to exercise in 13 angiographic collaterals ($43.7 (3.4)$ to $66.6 (8.5)$ ml/100g/min, $p < 0.005$) and 11 "collaterals" seen with xenon ($30.2 (7.9)$ to $57.5 (9.3)$ ml/100g/min, $p < 0.005$). Regional left ventricular function, measured by percentage shortening, was preserved in these patients (mean $38.9 (3.9)\%$). Flow was maintained on exercise in six angiographic collateral distributions ($45.7 (5.3)$ and $44.7 (6.3)$ ml/100g/min) and nine xenon collaterals ($39.0 (7.6)$ and $38.4 (3.3)$ ml/100g/min), as was regional left ventricular function $38.8 (4.0)\%$. In six collaterals seen angiographically flow fell after exercise from $50.3 (7.6)$ to $35.3 (7.4)$ ml/100g/min ($p < 0.01$), and in 10 xenon distributions it fell from $47.5 (6.4)$ to $24.7 (5.9)$ ml/100g/min ($p < 0.01$). In comparison with distribution where flow increased or was maintained on exercise (percentage shortening $38.8 (2.8)\%$), in regions where collateral flow fell, regional left ventricular function was impaired ($25.6 (2.8)\%$, $p < 0.01$). Thus, collateral flow which is maintained on exercise appears to be of value in preserving regional left ventricular function.

Percutaneous balloon dilatation of right ventricular outflow tract and pulmonary valve in patients with tetralogy of Fallot

J G C Wright, R Arnold, R M Bini, J L Wilkinson,
D I Hamilton, R McKay
Royal Liverpool Children's Hospital

Percutaneous balloon dilatation is successful in the treatment of isolated pulmonary valve stenosis and pulmonary artery branch stenosis. This encouraged us to perform percutaneous balloon dilatation of the right ventricular outflow tract and pulmonary valve in 21 symptomatic patients (aged 12 days to 18 years) with tetralogy of Fallot between December 1983 and December 1985. Eleven patients were infants under one year of age (group I). Before balloon dilatation two patients needed prostaglandin infusion to maintain ductal patency, five suffered cyanotic spells, and four had persistent severe cyanosis. After balloon dilatation palliative operation was obviated in 10 patients and the remaining patient required a Waterston anastomosis. Of the ten older patients (group II), exercise tolerance was improved and cyanosis reduced in three and hypoxic spells were abolished in one. The remaining six patients were not

significantly improved. Balloon dilatation was well tolerated by all patients. One patient from group I and five from group II have subsequently had open heart surgery. The operative findings relating to the pulmonary valve were: commissural splitting in three, a flail anterior cusp in two, and a central tear of the right pulmonary cusp in one.

This preliminary report suggests that balloon dilatation in patients with tetralogy of Fallot can be performed safely; it may obviate the need for palliative surgery but is of limited use in older patients.

Doppler echocardiographic determination of flow from five cardiac locations: a comparison with thermodilution

B A MacLennan, C Maguire, N P S Campbell
Regional Medical Cardiology Centre, Royal Victoria Hospital, Belfast

In patients without intracardiac shunts or valvar insufficiency, measurement of flow from several intracardiac locations would increase confidence in values obtained by non-invasive Doppler echocardiography. The purpose of this study was to correlate volume flow, estimated from five cardiac sites by range gated pulsed Doppler techniques, with simultaneous thermodilution flow measurements. Nineteen patients, 17 men and two women, aged 35–65 (mean 50.6) years, all with ischaemic heart disease and undergoing coronary arteriography, were studied. Ascending and descending aorta, main pulmonary artery, mitral and tricuspid inflow areas were interrogated for optimal Doppler signals. Vessel and valve orifice dimensions were obtained directly from cross sectional echocardiographic images. Doppler velocity signals were obtained from the ascending aorta in 19 patients (100%), from descending aorta in 18 (95%), pulmonary artery in 12 (63%), from tricuspid inflow in 12 (63%), and from mitral inflow in 18 (85%) patients. Velocity signals from all five sites were obtained in nine patients (47%). Significant correlations with thermodilution were obtained from ascending ($r=0.69$) and descending ($r=0.72$) aortic and pulmonary artery ($r=0.65$) derived flows. The poorest correlation resulted from using mitral and tricuspid orifice derived flows.

This study demonstrates that Doppler derived aortic and pulmonary flows correlate well with thermodilution flow measurements. When quantifying intracardiac shunts or valvar insufficiency by Doppler techniques, atrioventricular valve derived flow should be avoided.

Identification of anatomically and functionally severe coronary artery disease by the ST segment/heart rate slope

P Kligfield, P M Okin, O Ameisen, J S Borer
New York Hospital-Cornell Medical Center

To test the ability of the exercise ST segment/heart rate slope (ST/HR slope) to identify anatomically and functionally severe coronary disease, 84 consecutive patients with stable angina referred for coronary angiography were prospectively evaluated by a treadmill protocol designed to produce small heart rate increments between stages. The ST/HR slope, partitioned at $6 \mu\text{V}/\text{beat}/\text{min}$ in accord with previous studies, identified three vessel disease with a sensitivity of 94% (31/33) and a specificity of 63% (32/51). When three vessel disease was not present, steep ST/HR slopes identified otherwise important obstruction. Among patients with coronary disease, the anatomical extent of obstruction assessed by Gensini score was significantly greater in 47 patients with ST/HR slopes >6 than in 25 patients with slopes <6 (65 (5) *vs* 25 (4), $p<0.0001$). This was not explained by the greater number of obstructed coronary arteries found in patients with higher ST/HR slopes since among 39 patients with only one or two vessel disease the mean Gensini score was also higher in patients with slopes >6 (56 (8) *vs* 24 (4), $p<0.0002$). In addition the mean exercise induced fall in ejection fraction determined by radionuclide cineangiography in 36 patients was significantly greater in patients with slopes >6 (-7 (2) *vs* -1 (2)%, $p<0.05$). These data demonstrate that an ST/HR slope $>6 \mu\text{V}/\text{beat}/\text{min}$ is a highly sensitive means of identifying three vessel coronary disease and that this partition value accurately identifies additional patients with angina who have anatomically or functionally extensive coronary obstruction.

False positive ST segment depression during post-myocardial infarction exercise testing

L B Tan, D P Murray, P L Weissberg, M Salih, R G Murray, W A Littler
University of Birmingham Department of Cardiovascular Medicine

Electrocardiographic ST segment depression during exercise tests after myocardial infarction (MI) sometimes does not correlate with the location of coronary

artery narrowing and the myocardium in jeopardy. Such ST depression is commonly termed false positive ST depression. No systematic study of false positive ST depression during post-MI exercise tests has been reported. Ninety patients with a positive 12 lead predischARGE exercise test after acute MI had coronary angiography six to 12 weeks after discharge. ST segment depression in discrete ECG groupings was used to predict individual vessel disease. Twenty eight patients displayed false positive ST depression, that is no important stenosis of the suspected coronary artery. Of these, 15 had exercise induced ST elevation in the infarcted area and 15 had true posterior infarction (five were common to both groups), indicating that in these 25 patients the ST depression observed could be explained by the reciprocal electrical phenomenon. The remaining three patients had no identifiable reciprocal ST changes, but the suspect vessels all donated large collaterals to the infarcted zone suggesting a coronary steal phenomenon. During follow up (mean 12 months) those with false positive ST depression had fewer cardiac events (37% *vs* 87%, $p < 0.05$), including angina (37% *vs* 87%, $p < 0.05$) and further myocardial infarction (0% *vs* 18%, $p < 0.05$) than those with true positive exercise tests. In conclusion, false positive ST depression was common during post-MI exercise tests, and may be explained by reciprocal ST changes and/or the coronary steal phenomenon. Such patients had a better prognosis compared with those who had a true positive exercise test.

The significance of ST segment depression in syndrome X assessed by ambulatory pulmonary artery pressure monitoring

R Levy, L M Shapiro, C Wright, L Mockus, K M Fox
National Heart Hospital, London

The pathophysiology and clinical importance of anginal chest pain with a positive exercise test and normal coronary arteriography (syndrome X) are poorly understood. The purpose of this study was to determine the relation between chest pain, ST segment depression, and changes in left ventricular function assessed by the measurement of ambulatory pulmonary artery diastolic pressure (PADP) with simultaneous frequency modulated ECG in patients with syndrome X. The PADP was measured during treadmill exercise and throughout ambulatory 24 hour monitoring in unrestricted subjects; six

patients with syndrome X (mean age 48 (12) years) were compared with six controls (mean age 39 (7) years) and 19 patients with coronary artery disease (mean age 57 (11) years). On treadmill exercise in both syndrome X and in normal controls there was no significant rise in PADP despite ST segment depression (range 1–4.5 mm) in the former group. In coronary artery disease, however, on exercise there was a rise in PADP of a median 5 mmHg (range 0–13.6 mmHg). In only one patient with coronary artery disease was there no rise in PADP, despite 1 mm ST segment depression. During ambulatory monitoring in patients with syndrome X, 12 episodes of ST segment depression (1 mm) were observed (four painful, eight painless) in which there was no change in PADP. This differs from 29 anginal episodes in coronary artery disease in which there was a significant ($p < 0.01$) rise in PADP of a median 7.5 mmHg (range 1.8–19.7 mmHg). Chest pain and ST segment changes in patients with syndrome X do not appear to be associated with impaired left ventricular function assessed by ambulatory pulmonary artery pressure monitoring. This differs markedly from the haemodynamic changes during myocardial ischaemia in coronary artery disease.

Diurnal variation in pulmonary artery diastolic pressure: a mechanism for early morning myocardial ischaemia

R D Levy, L M Shapiro, A D Cunningham, C Wright, L Mockus, K M Fox
National Heart Hospital, London

Patients may present with angina pectoris in the early morning. The mechanism of this is unclear and both haemodynamic changes and coronary artery spasm may be important. The purpose of this study was to investigate the diurnal variation in pulmonary artery diastolic pressure (PADP), reflecting left ventricular end diastolic pressure (LVEDP), in five normal subjects (mean age 39 (6.6) years), 18 patients with coronary artery disease (CAD) (mean age 57 (11) years), five patients with coronary artery spasm (mean age 51 (8) years), and six patients with syndrome X (mean age 48 (12) years). Ambulatory 24 hour recordings of PADP were obtained with a transducer tipped catheter and a simple recording system and were related to the timing of episodes of ST segment depression and elevation by simultaneous frequency modulated ECG recording. This

system avoids the problems of a zero reference point commonly found with fluid filled catheters and external transducers. Episodes of ST segment change occurred predominantly in the early morning (4–8 am) in coronary artery spasm (seven out of 14 episodes), whereas in syndrome X all episodes occurred during the daytime, and in coronary artery disease painful and painless episodes were distributed throughout the day with 15 out of 67 occurring between midnight and 8 am. In all groups a similar diurnal variation in PADP was observed with a tendency for low values during the day and higher values at night with the maximum values occurring between midnight and 6 am. These findings that pulmonary artery diastolic pressure and therefore LVEDP are greatest in the early morning may suggest a new mechanism for the increased susceptibility to myocardial ischaemia during these hours.

The effect of β receptor antagonist therapy on the diagnostic accuracy of non-invasive tests used in the detection of coronary artery disease

T Crake, A A Quyyumi, C Wright, L Mockus, K M Fox
National Heart Hospital, London

Exercise testing and ambulatory ST segment monitoring are used in the assessment of patients with coronary artery disease. These investigations are often performed while patients are taking anti-anginal agents but their reliability during treatment with β blockers is unknown. The effects of β blockade were investigated in 34 patients with coronary artery disease who had positive exercise tests and episodes of ambulatory ST segment depression while they were not on antianginal medication. After β blockade 17 patients had no ambulatory ST segment changes (sensitivity reduced to 50%). In the remaining 17 patients the frequency, duration, and magnitude of ST segment change, whether painful or painless, were significantly reduced ($p < 0.01$). Mean exercise duration was increased by 73% ($p < 0.01$) with β blocker treatment. Exercise tests became negative in only two patients after β blockade (sensitivity 94%). Before β blockade 70% of patients with three vessel disease ($n = 20$) developed a positive exercise test within the first stage of treadmill exercise on the modified Bruce protocol; after β blockade only 17% of this group of patients had positive exercise tests at this stage.

Thus the administration of β blockers reduces the sensitivity of both exercise testing and ambulatory ST segment monitoring in the detection and evaluation of coronary artery disease. However, the effects on ambulatory ST segment monitoring are much more profound.

Symptom limited exercise and respiratory gas exchange in heart failure

J G F Cleland, K W Stirling, Esther Henderson, H J Dargie
Cardiac Department, Western Infirmary, Glasgow

It has been suggested that measurement of ventilatory capacity and gas exchange can be helpful in the assessment of cardiac impairment. In many subjects with heart failure exercise capacity is limited not by breathlessness but by fatigue which may vary according to the protocol—for example the speed and inclination of the treadmill. The purpose of this study was to investigate the effects of two different exercise protocols on symptoms and gas exchange when they were tested in random order in 20 patients (age 58 (11) yr) with heart failure due to left ventricular dysfunction (NHYA class II–III). The slow test had two minute stages at 1 mph/0%, 1.5/0, 1.5/4, 2/4, etc, and the fast test had one minute stages at 1/0, 1.5/4, 2/8, etc. Exercise time was 681 (233) s for slow and 289 (70) s for fast tests ($p < 0.001$). Ventilation (46 (14) vs 54 (13) l/min; $p < 0.001$), respiratory rate (29 (6) vs 32 (6) breaths/min; $p < 0.02$), heart rate (125 (20) vs 131 (18) beats/min; $p < 0.005$), and systolic blood pressure (143 (28) vs 154 (38) mm Hg; $p < 0.01$) were all higher at peak exercise with the fast test, as were maximal oxygen consumption (14.4 (5.5) vs 16.4 (5.0) ml/kg/min; $p < 0.005$) and respiratory exchange ratio (1.06 (0.21) vs 1.17 (0.17); $p < 0.005$). Anaerobic threshold was reached in only 11 patients with the slow test but in 18 with the fast test. But when only the results of the tests in those attaining the anaerobic threshold were compared the above differences were maintained. With the fast test 17 subjects stopped with breathlessness as the principal symptom compared with eight on the slow test ($p < 0.01$). The use of a single standard exercise protocol to assess cardio-respiratory function for patients with heart failure of differing severities may be inadequate. In particular anaerobic threshold will not be achieved in about half the patients during a slow protocol, and this will lead to a considerable underestimation of their exercise capacity.

Mechanisms of closure of perimembranous ventricular septal defects: a cross sectional and pulsed Doppler echocardiographic study

U S V Balam, S Karas, K A Hallidie-Smith
Royal Postgraduate Medical School, London

Pathological and surgical studies have shown that spontaneous closure of defects encroaching on the membranous ventricular septum (perimembranous) is less frequent than those in the muscular septum, but that there is a tendency for a good proportion of them to diminish in size, with complete closure occurring in some of them. However, the actual mechanism responsible for the partial or complete closure of these defects remains controversial. In this study the incidence and the various mechanisms involved in closure have been documented by cross sectional echocardiography and pulsed Doppler echocardiography.

Eighty five successive patients (aged from one day to 25 years) with perimembranous defects, defined by cross sectional echocardiography were studied. The age range of these patients is as follows: <1 year, 16; 1 to 5 years, 22; 6 to 10 years, 30; 11 to 16 years, 7; >16 years, 10. Thirty four (40%) of the defects showed some evidence of closure, with 28 being trabecular, three inlet defects, none in the outlet septum, and three of the confluent type. The anatomical structures responsible for the reduction in size or closure of these defects are (a) subtricuspid valve apparatus (24/34 cases, 70%), (b) bridging of septal tricuspid leaflet across the defect (7/34 cases, 20%), and (c) prolapse of the aortic leaflet (3/34 cases, 9%). In none of the cases was aneurysm of the membranous septum noted. Pulsed Doppler echocardiography showed systolic flow turbulence across the residual defect from left to right ventricle in all cases in (a) and four of seven cases in (b). Turbulence was noted both in the right atrium and right ventricle because of the bridging tricuspid septal leaflet across the defect. In three of seven of this group no flow was detected as the defect was completely closed by the septal tricuspid leaflet. In (c) all cases had evidence of aortic regurgitation as shown by diastolic flow turbulence.

From this attempt to analyse the incidence, mechanisms of closure, and residual flow jets in perimembranous ventricular septal defects by cross sectional echocardiography and pulsed Doppler echocardiography it is concluded that the tricuspid valve apparatus is the most important anatomical structure for the closure of these defects. Aneurysm of the membranous septum did not occur in this series.

Left ventricular structure and function in bodybuilders

I C Todd, G McKillop, D Ballantyne
Victoria Infirmary, Glasgow

Isometric exercise is known to induce cardiac muscle hypertrophy as well as skeletal muscle hypertrophy. Bodybuilding has the unique aim of inducing muscular enlargement and definition per se rather than of improving strength. It might also be expected to induce more cardiac enlargement than other isometric exercise. In addition, the use of anabolic drugs is widespread among bodybuilders, but little is known of their cardiac effects. Eighteen male bodybuilders and nine matched controls were studied by cross sectional echocardiography. Nine of the bodybuilders used anabolic drugs. The athletes were found to have significantly greater posterior left ventricular wall and septal thickness than controls, and left ventricular mass values were higher than previously reported for any athletes. In addition their left ventricular volumes were increased and ejection fractions were significantly reduced. The bodybuilders who used anabolic drugs had higher values than those who did not; but the only significant difference was for posterior wall thickness. Exercise induced cardiac hypertrophy is believed to mirror skeletal muscle hypertrophy and may be augmented by the use of anabolic drugs. In the presence of commonly used high calorie atherogenic diets there is a potential for the development of early cardiac ischaemia.

Acromegalic heart disease: clinical features and results of treating the acromegaly

R Hayward, R Emanuel, J D N Nabarro
Departments of Cardiology and of Medicine,
Middlesex Hospital

The clinical features and prognosis of acromegalic heart disease remain ill-defined. Fifty eight (23%) of 256 acromegalic patients referred to one centre had heart disease diagnosed because of the presence of cardiomegaly, abnormal electrocardiogram, or arrhythmia. In 10 (4%) of them acromegaly was the sole cause. In the remaining 19% hypertension, ischaemic and rheumatic heart disease, and thyrotoxicosis contributed, and the diagnosis was of secondary cardiac disease. Eight of those with acromegalic heart disease had left ventricular dilatation and hypokinesia (ejection fractions 24–46%), two showed concentric hypertrophy and high ejection

fractions, one with a mid-cavity gradient. Coronary arteriograms, which were performed in seven cases, showed no obstructions, but the coronary arteries were large in three. Acromegaly was cured by pituitary surgery or radiotherapy or both in six patients who were followed up for 1–11 (mean 9) years. Left ventricular function has improved in only two, deteriorated in two, and in one the gradient has resolved. Four have developed new arrhythmias but none has died of heart disease after cure of acromegaly. Cure was not achieved in four; one has been lost to follow up and three have died of cardiac failure 1–5 years after detection of heart disease.

The manifestations of acromegalic heart disease are not consistent and most cardiac disease in acromegaly stems at least partly from associated conditions. Cure of acromegaly can retard or reverse heart disease, particularly muscle dysfunction, but is often too long delayed.

Haemodynamic function over five years after orthotopic cardiac transplantation

A G Mitchell, M H Yacoub
Harefield Hospital, Harefield, Middlesex

The annual haemodynamic investigations following orthotopic cardiac transplantation have been reviewed from January 1980. Numbers of patients from 1–5 years were 91, 33, 18, 6, and 3. Age at transplantation ranged from 14–56 years and seven were female. Immunosuppression was achieved using prednisolone and azathioprine in 14 or using cyclosporin and azathioprine with minimal or no steroids in 77. Nine late deaths occurred, eight of whom had steroid based immunosuppression. Resting haemodynamics for the group were right atrial (mean) 5.8(4) mm Hg; right ventricular systolic 28(7) mm Hg; RV end diastolic pressure 6.3(3) mm Hg; pulmonary arterial (mean) 18.3(5) mm Hg; RR interval 697(118) ms; left ventricular ejection fraction 69.3(16.6)%; pulmonary capillary wedge pressure (mean) 11.5(5) mm Hg; left ventricular systolic 132(23) mm Hg; LV end diastolic pressure 11.3(6) mm Hg; aorta (mean) 102(20) mm Hg; cardiac output 5.4(1.21)/min. None of these variables showed a significant trend over five years. Cyclosporin treatment was associated with hypertension (aorta mean 102(20) *vs* 92(15)) and longer RR interval (725(120) *vs* 635(96) ms). Left ventricular end diastolic pressure tended to be higher in patients with lower ejection

fractions, and those with over four episodes of rejection had worse left ventricular function than those with less than four episodes. Late deaths were associated with a reduction of ejection fraction and a rise of left ventricular end diastolic pressure. All had coronary disease at necropsy. Long term haemodynamic function after orthotopic cardiac transplantation requires prevention of acute and chronic rejection and appears independent of the method of immunosuppression.

Determinants of survival after repair of total anomalous pulmonary venous drainage

S A Qureshi, Rosemary Radley-Smith, M H Yacoub
Harefield Hospital, Harefield, Middlesex

Between June 1971 and April 1985, 28 patients underwent repair of total anomalous pulmonary venous drainage (TAPVD). The mean age at operation was 4 months (range 8 days to 1 year). Fifteen (54%) children were <3 months old. There were 22 males and six females, ranging in weight from 2.2 to 7.4 kg (mean 4.4 kg). Twelve (43%) patients had supracardiac, six (21%) intracardiac, five (18%) infracardiac, and five (18%) mixed TAPVD. Obstruction was present in 39% (11/28). Infants with obstructed TAPVD had a mean weight at operation of 3.4(0.65) kg and were operated on at a mean age of 1.43(1.9) months compared with a mean weight of 5.1(1.4) kg and a mean age of 5.8(3.7) months in the group with non-obstructed TAPVD. The overall operative mortality was 21% (6/28). The mortality was highest in (a) those aged <3 months of age, (b) those weighing <3 kg, (c) those with RV/LV ratio >1.0, and (d) in those with obstructed TAPVD. During a mean follow up of 55 months (range 6–144 months) there were two (7%) late deaths. All the survivors are symptom free, growing normally, and on no medication. Ten patients have undergone repeat cardiac catheterisation between two months and 11 years after operation. The pulmonary artery peak systolic pressure decreased from a preoperative mean of 64(35) mm Hg to 30(11) mm Hg postoperatively. There was no evidence of late pulmonary venous obstruction. Left ventricular function was normal in all the patients. Multivariate analysis showed that the strongest determinants of survival were sex, weight at operation, and pulmonary artery peak systolic pressure with age, anatomical type, presence of obstruction, RV/LV ratio, preoperative aortic saturation, and the year of operation having no significant influence on outcome.

Accelerated graft coronary arteriosclerosis after cardiac transplantation: can it be diagnosed non-invasively?

C J Reid, A G Mitchell, K Fox, M H Yacoub
Harefield Hospital, Harefield, Middlesex; and
National Heart Hospital, London

Severe coronary artery stenosis (CAS) due to diffuse intimal thickening is one of the potentially serious late complications of cardiac transplantation. Because of denervation angina does not occur; thus the development of reliable methods for detection of ischaemia in the transplanted heart is essential. In this study, several methods were assessed including stress testing, 24 hours ST segment monitoring, thallium scintigraphy, and radionuclide angiography. CAS was demonstrated at routine annual coronary arteriography and/or necropsy in 21 (19.8%) of 106 patients one or more years after cardiac transplantation. Eleven of these patients (group A) and 39 recipients with normal coronary arteriograms (group B) were studied. The mean (SEM) duration of treadmill exercise was 8.6 (1.52) min in group A and 10.6 (0.46) min in group B; HR \times BP was 21540 (3377) and 25184 (4973) respectively; ST change < 1 mm was observed in each group. In the 11 patients with CAS, thallium scintigraphy showed reversible ischaemia in one, a fixed defect in two, and normal perfusion in the remainder and in group B. Twenty four hour analysis showed transient 2 mm ST depression in one patient with CAS. Resting left ventricular ejection fraction by radionuclide angiography was 51.1 (4.64)% in group A increasing on exercise by 8.46 (2.48)%, compared with 62.1 (1.76)% and 12.3 (0.16)% respectively in group B. In conclusion, stress testing and ST segment analysis are not sensitive methods for detection of CAS after cardiac transplantation, whereas abnormal thallium scintigraphy and a resting ejection fraction $< 55\%$ are suggestive of this important late complication.

Sudden death in patients with supraventricular tachycardia terminating pacemakers

A J Camm, J Vohra, P Hesslein, E Cornu
St Bartholomew's, London; Royal Melbourne,
Melbourne; Sick Children's, Toronto; and Telec-
tronics, London

PASAR 4151 (Teletronics) is an automatic fully implantable device which is designed to terminate tachycardia by the introduction of one or two premature beats. Worldwide 122 were implanted for the control of supraventricular tachycardia—70 for atrioventricular reentrant tachycardia (AVRT), 42 for AV nodal reentrant tachycardia (AVNRT), and 10 for other tachycardias. Over a total follow up period in excess of 2500 patient months there have been four sudden deaths: (a) a girl (aged 13) with Wolff-Parkinson-White syndrome (WPW) type A (refractory period, 270 ms) and orthodromic AVRT (193 beats/min) treated with two ventricular premature beats; (b) a woman (aged 52) with WPW type A (refractory period, 260 ms) and orthodromic AVRT (200 beats/min) terminated by two ventricular premature beats; (c) a man (aged 69) with ischaemic heart disease and AVNRT (170 beats/min) terminated with two atrial premature beats (coronary sinus); (d) a young girl with AVNRT (190 beats/min) and a nodoventricular connection treated with double right atrial stimulation. In this last patient Holter ECG recording at the time of death demonstrated seemingly spontaneous initiation of atrial fibrillation with a rapid, preexcited ventricular response (up to 375 beats/min). The role of PASAR was not apparent. The occurrence of sudden death has been unacceptably high. Possible associations include: WPW syndrome, short anterograde refractoriness of the accessory pathway, ischaemic heart disease, ventricular pacing, and the use of two premature beats, all of which should be avoided when considering the use of a pacemaker to terminate tachycardia.

Place of antiarrhythmic therapy in acute myocardial infarction?

A J McLintic, Ann Tweddel
University Department of Medical Cardiology,
Royal Infirmary, Glasgow

Coronary care unit policy in 1974, when antiarrhythmic treatment was regularly prescribed, was compared with policy in 1984 when in general it was no longer given. The in hospital mortality has remained unchanged—16% in 1974 and 15.5% in 1984. In 1974, 108 (37%) of 295 patients with proven myocardial infarction were treated with antiarrhythmic agents for ventricular extrasystoles (VES) occurring ≥ 1 in 5, couplets, multifocal, or as R on T. In 1984 only 2% of patients were treated

with these agents. The incidence of ventricular tachycardia has risen from 4% to 18% ($p < 0.001$) and ventricular fibrillation from 5% to 19% ($p < 0.001$). Of the patients with ventricular fibrillation, 6% had prodromal VES in 1974 and 10% had them in 1984. The incidence of primary ventricular fibrillation was similar in 1974 and 1984 (4% and 8% respectively). The in hospital mortality in those patients with ventricular fibrillation was not significantly different (1% to 5%). Death from ventricular fibrillation was associated with left ventricular failure (80%) and tended to occur later than 72 hours after onset of symptoms (80%).

In conclusion, a change in policy in the treatment of ventricular arrhythmias has not affected in hospital mortality in patients with acute myocardial infarction, and mortality is related to failure of pump function rather than to electrical events.

Recognition of ventricular tachycardia and ventricular fibrillation from the timings of epicardial electrograms

D W Davies, R J Wainwright, S R Large,
S J Edmondson, G M Rees, A J Camm
St Bartholomew's and the Brook Hospitals, London

Recurrent ventricular tachycardia (VT) and ventricular fibrillation (VF) are increasingly treated by implantable cardiac defibrillators capable of delivering DC shocks between two epicardial patch electrodes. A major problem with such devices is the difficulty of recognising ventricular arrhythmias, especially VF. The possibility that VT and VF could both be distinguished from sinus rhythm and from each other by epicardial signals was therefore assessed. Ten patients undergoing elective coronary artery surgery were studied. Bipolar electrograms from four epicardial (left and right ventricular apical and paraseptal) sites were recorded simultaneously for the initial minutes of normothermic cardiopulmonary bypass during control rhythm (nine sinus, one atrial fibrillation), right ventricular pacing (to simulate VT) at three pacing rates (120, 150, and 180 beats/min), and VF induced by AC current. Control heart rates varied from 65 to 130 (mean 91) beats/min. Within each control and paced rhythm the electrograms from the four sites occurred in a stable sequence, but the sequence differed between the two rhythms in eight patients. With ventricular pacing the time from first to last electrogram increased by 40 to 90 (mean 65). Varying the pacing

rate did not affect this time nor the electrogram sequence. During VF, rapid irregular localised intrinsic activity was seen at all four sites, with cycle lengths ranging from 130 to 240 ms and with signal amplitudes ranging from 0.4 to >5 times those obtained during control rhythms. Complete asynchrony of the four sites was present during VF. Detection of a different sequences and timing of multiple epicardial electrograms will allow automatic recognition of VT, and complete asynchrony of the electrograms indicates the onset of VF.

Increase in S wave amplitude during transient myocardial ischaemia

J J Glazier, S Chierchia, A Margonato, A Maseri
Cardiovascular Unit, Hammersmith Hospital, London

A consistent association between exercise induced ST segment depression and an increase in S wave amplitude has been observed. To investigate this phenomenon further, 30 high quality 24 hour Holter tapes recorded in 15 patients with chronic stable angina and important coronary artery disease were analysed. Eleven patients also underwent continuous ECG recording (12 leads) along with cross sectional echocardiography during acute myocardial ischaemia induced by intravenous dipyridamole. During Holter monitoring 157 episodes of diagnostic ST depression (0.19 (0.09) mV, mean (SD)) were detected which were invariably associated with an increase in S wave amplitude (0.23 (0.14) mV), whereas no consistent change in R wave amplitude was observed. The increase in S wave usually (70% of episodes) preceded the onset of ST depression and was quantitatively related to the severity of ST depression. For the different severity subgroups of ST depression ≥ 0.1 and < 0.2 mV, ≥ 0.2 and < 0.3 mV, and ≥ 0.3 mV, the mean increases in S wave amplitude were 0.20 (0.09) mV, 0.27 (0.14) mV, and 0.32 (0.11) mV respectively (analysis of covariance, $p < 0.01$). Fourteen episodes of an isolated increase in S wave amplitude without diagnostic ST depression occurred; two of them were associated with angina. During dipyridamole induced ischaemia all 11 patients developed transient regional wall motion abnormalities which were associated with diagnostic ST depression (0.15 (0.02) mV) and angina in nine and with an increase in S wave amplitude in all.

It is concluded that (a) an increase in S wave

amplitude is consistently associated with acute myocardial ischaemia; and (b) in some cases changes in S wave could be more sensitive than classic ST segment variables for detecting acute myocardial ischaemia.

Epicardial repolarisation mapping in man

J C Cowan, C J Hilton, C J Griffiths, J Bourke, S Tansuphaswadikul, A Murray, R W F Campbell
Freeman Hospital, Newcastle upon Tyne

Dispersion of repolarisation has been postulated as a mechanism of arrhythmogenesis, but methods for its measurement in man have remained inadequate. A new technique of epicardial repolarisation mapping is described. Monophasic action potentials were recorded intraoperatively by a specially designed hand held silver/silver chloride electrode applied to the epicardium. Recordings were obtained during fixed rate atrial pacing from 53 epicardial points. For each epicardial position activation time, repolarisation time, and action potential duration were determined. Repolarisation maps were plotted in four patients without a history of arrhythmias or myocardial infarction who were undergoing coronary bypass grafting. The number of points giving acceptable stable recordings varied between 21 and 38 in different patients. The dispersion of repolarisation times was 86(9) (mean(SD)) ms. Repolarisation time correlated significantly with action potential duration (mean correlation coefficient, $\bar{r}=0.67$), but not with activation time ($\bar{r}=0.23$). An inverse relation was observed between activation time and action potential duration ($\bar{r}=0.54$), reducing the observed dispersion of repolarisation times.

In conclusion, the technique of epicardial monophasic action potential recording offers considerable promise as a means of studying the role of repolarisation abnormalities in arrhythmogenesis in man. Preliminary observations in a small number of patients without a history of arrhythmias have shown an inverse relation between activation time and action potential duration. This may reduce dispersion of repolarisation and may represent a protective mechanism.

Influence of R wave amplitude and Q waves on exercise induced ST segment depression

P R Walker, M Papouchado, J R Fraser, R P H Wilde
Departments of Cardiology and Radiodiagnosis, Bristol Royal Infirmary, Bristol

Conflicting results have been obtained from recent studies in which the precise depth of ST segment depression during exercise has been used to predict the arteriographic severity of coronary artery disease (CAD). However, these studies have largely overlooked the influence of R wave amplitude or Q waves on ST depression. In this study 114 patients with CAD were subgrouped, firstly according to the presence or absence of Q waves and secondly according to the greatest R wave amplitude in their resting ECG. As assessed by a myocardial scoring technique the arteriographic severity of CAD was slightly greater among 26 patients with Q waves than among 88 patients with no Q waves; however, the mean maximum depth of ST depression during exercise testing was 41% greater in patients with no Q waves (1.66(0.92) mm *vs* 1.18(0.97) mm, $p<0.05$). The influence of R wave amplitude was even more striking. Thirty four patients had tall (≥ 20 mm) R waves, 52 had medium sized (13–19 mm) R waves, and 28 had small (≤ 12 mm) R waves. The mean myocardial scores were similar in the three groups, the small R wave group having the highest score. However, the tall R wave patients exhibited twice the depth of ST depression seen in small R wave patients (2.04(0.95) mm *vs* 1.03(0.80) mm, $p<0.0005$); whereas the medium sized R wave patients showed an intermediate amount of ST depression (1.51(0.88) mm). Similar maximum heart rates were achieved by all five subgroups analysed.

Because of the influence of R wave amplitude and Q waves ST segment depression alone would not be expected to predict the severity of CAD.

External non-invasive temporary cardiac pacing

E Rosenthal, Susan Lewis, I Sram, N Thomas, S Ikram, R Vincent, D A Chamberlain
Royal Sussex County Hospital, Brighton, Sussex

Transcutaneous cardiac pacing, introduced by Zoll in 1952, has attracted a resurgence of interest because longer stimulus duration and larger electrodes now permit lower stimulation thresholds. The usefulness of the Pace Aid (pulse width 20 ms, output 50, 100, or 200 mA; Cardiac Resuscitator Corporation) and the Zoll NTP non-invasive temporary pacemaker (pulse width 40 ms, output 0–140 mA; Simonsen and Weel) has been assessed. Transcutaneous pacing was attempted in 46 patients (age range 17–84)—14 with stable complete heart block, 10 with severe bradycardia and hypotension, and 22 with asystole. Transcutaneous pacing restored output in 11 patients—six with stable complete heart block, four with bradycardia and hypotension, one in asystole. In four patients the Zoll NTP created artefacts after the pacing stimulus that resembled a QRS complex but were not associated with a repolarisation wave or cardiac output. This simulates electromechanical dissociation and can cause delay in initiation of traditional resuscitation methods. External pacing was uncomfortable for conscious patients and none was able to tolerate maximal electrical output, even after intravenous sedation. A rise in pacing threshold over the course of an hour with a loss of capture was noted in one patient. Transcutaneous pacing may occasionally restore cardiac output in patients with severe bradycardia. But it proved disappointing with asystole and unreliable and uncomfortable in conscious patients with stable bradycardias. It is of limited value in the treatment of cardiac emergencies.

Left ventricular false tendons in man: identification of clinically significant morphological variants

J M Beattie, F A Gaffney, L M Buja, C G Blomqvist
University of Texas Southwestern Medical School,
Dallas, Texas, USA

Left ventricular false tendons are composed of Purkinje fibres and are intracavitary branches of the peripheral conduction system of the heart. Their clinical importance is unknown. Their morphological variation in 167 unselected diseased hearts was examined at necropsy and in 2004 consecutive patients examined by cross sectional echocardiography. Left ventricular regions were defined as apical, mid-ventricular, or basal. False tendons arising and inserting within the same ventricular

region were classified as transverse, between two adjacent regions as diagonal, and traversing all three regions as longitudinal. False tendons were identified in 29 hearts (17%) in the necropsy group and in 81 patients (4%) in the echocardiographic group. Relative prevalences in the necropsy and echocardiographic groups respectively were: apical transverse (2 and 32), mid-ventricular transverse (12 and 21), apical/mid-ventricular diagonal (4 and 9), and mid-ventricular/basal diagonal (19 and 23). No longitudinal false tendons were noted. Echocardiography underestimated the occurrence of these structures which were usually an incidental finding. However, the largest clinical subset comprised 17 patients, 10 presenting with atypical chest pain and murmur and 7 with asymptomatic murmur, in whom the presence of false tendons was the only echocardiographic feature noted. This association was highly significant ($p < 0.001$). Thirteen of this group exhibited transverse morphology, with mid-ventricular location predominating ($p < 0.01$). This morphological variant, lying perpendicular to the left ventricular outflow tract, is particularly subject to traction and by disturbing intracardiac flow patterns may result in this clinical presentation.

Characterisation of the normal right ventricular pressure-volume loop using biplane ventriculography and simultaneous high fidelity pressure measurement

A N Redington, M L Rigby, M E Hodson,
P J Oldershaw
Brompton Hospital, London

To characterise the normal right ventricular (RV) pressure-volume (P-V) loop, biplane right ventriculography with simultaneous high fidelity pressure recordings were performed in adult patients considered to have a normal RV and normal coronary arteries at cardiac catheterisation and angiography. RV volume was measured by a modification of Simpson's rule. To validate this method of RV volume measurement, 22 radioopaque casts from necropsy human and animal right ventricles were made. The calculated volume (V_c), determined from hand digitised frontal and lateral "ventriculograms" of the casts, was compared with true volume (V_t) measured by fluid displacement. Excellent correlation was obtained after adjustment of V_c by the regression equation $V_t = 0.86 V_c + 0.68$ ($r = 0.99$, SEE(4)). Frame by frame analysis of right ventriculograms

obtained at catheterisation thus enabled the generation of a simple volume-time curve from which the P-V loop was derived. Fundamental differences were found between normal RV and left ventricular (LV) P-V loops. The normal RV P-V loop was more triangular in shape with ejection beginning during pressure upstroke. Consequently there was no well defined period of isovolumic contraction. Furthermore RV volume continued to decrease well beyond peak RV pressure, up to 60% of the stroke volume being ejected during RV pressure fall. These differences may reflect the low impedance to pulmonary flow.

In conclusion, the normal RV P-V loop was significantly different from that of the normal LV; this observation has important implications when considering isovolumic or end systolic indices of RV contractility.

Phase and amplitude analysis of exercise digital left ventriculograms: a new method of detecting myocardial ischaemia

J Lyons, M Norell, J Gardener, R Balcon, C Layton
London Chest Hospital

Phase and amplitude analysis of digital left ventriculograms allows assessment of wall motion while avoiding the artefacts associated with image subtraction. Intravenous digital left ventriculography was performed in 23 patients with known coronary artery disease (CAD): eight with one vessel disease, 11 with two vessel disease, and four with three vessel disease. Images were obtained at 12.5 frames/s in a right anterior oblique projection after a right atrial injection of contrast. Patients then performed a symptom limited supine bicycle exercise test. A second ventriculogram was obtained at peak exercise. The resultant images were subjected to phase and amplitude analysis, and assessed blindly in random order, with the ventricle considered as three segments. All ventricles were found to be abnormal at rest, despite normal cineangiograms in eight patients. In all but one, the wall motion abnormalities were consistent with the CAD. On exercise, five patients showed no change in wall motion; all had one vessel disease. In 13 patients there was a deterioration in wall motion affecting a previously normal segment in six and an abnormal one in seven; this group contained all four patients with three vessel disease and six with two vessel disease. In five

patients, all with two vessel disease, there was either a discrepancy between the abnormal segments at rest and on exercise, or apparent improvement in wall motion of one segment.

Phase and amplitude analysis of digital left ventriculograms is a method of assessment of exercise induced ischaemia that is simple to perform, has high resolution, and is a sensitive detector of severe CAD.

Plasma catecholamine secretion during cardiac surgery: a double blind comparison of trimetaphan camsylate with sodium nitroprusside

Laura Corr, R M Grounds, J G Whitwam,
M J Brown
Royal Postgraduate Medical School, London

Cardiopulmonary bypass has been shown to be a potent stimulus to the release of catecholamines and may be associated with a high systemic vascular resistance. Furthermore the concentrations of circulating plasma catecholamines reported may have important metabolic effects. The effects of trimetaphan camsylate (TC) and sodium nitroprusside (SNP) on the catecholamine response to cardiac surgery were compared in a randomised, double blind study of 12 male patients undergoing elective myocardial revascularisation. The solutions were titrated to maintain a mean arterial pressure of 70–85 mm Hg before and after bypass and <70 mm Hg during bypass. The rise in plasma adrenaline in the SNP group during cardiopulmonary bypass (0.019 (0.007) ng/ml to 1.058 (0.228) ng/ml) was much greater than in the TC group (0.018 (0.007) ng/ml to 0.261 (0.136) ng/ml; $p < 0.02$ between groups). There was a smaller rise in plasma noradrenaline in the SNP patients (0.482 (0.098) ng/ml to 2.933 (0.8) ng/ml) but this was significantly higher than in the TC patients (0.484 (0.16) ng/ml to 1.286 (0.511) ng/ml; $p < 0.05$ between groups). The plasma potassium and glucose concentrations in the two groups were also compared. Plasma potassium fell initially on bypass in the SNP group (4.34 (0.08) to 4.0 (0.16) mmol/l) but did not fall in the TC group (4.23 (0.15) to 4.20 (0.18) mmol/l). Thereafter plasma potassium tended to rise in both groups but remained lower throughout operation in the SNP patients ($p < 0.02$). Plasma glucose rose in the TC group (to 6.53 (0.21) mmol/l) but the rise in SNP group was significantly higher (to 9.48 (0.82) mmol/l; $p < 0.05$ between groups).

The use of TC provides a simple and effective way to reduce catecholamine release during cardiopulmonary bypass. The haemodynamic benefits of vasodilation are obtained and the metabolic consequences of high circulating catecholamines are avoided.

Free radical generation in coronary and peripheral vascular disease

S Hutchison, J Belch, E Smith, C Forbes, A R Lorimer

Department of Medical Cardiology, Royal Infirmary; and Department of Chemistry, Strathclyde University, Glasgow

Oxygen free radicals (FR) may be important mediators of tissue damage in pathological states involving inflammation and ischaemia. Methods to assess changes in the cell defence to free radical generation have been developed—such as measurement of glutathione concentration and superoxide dismutase activity. Raised concentrations of glutathione and decreased concentrations of superoxide dismutase correlate with increased free radical generation. Glutathione and superoxide dismutase were measured in 26 patients with arterial disease and the results compared with those in 17 matched controls. Superoxide dismutase concentrations were significantly lower in patients with arterial disease (48 (7) $\mu\text{g}/\text{ml}$ in patients with angina ($p < 0.02$), 44 (6) $\mu\text{g}/\text{ml}$ in patients with claudication ($p < 0.01$)) than in normal individuals (71 (5) $\mu\text{g}/\text{ml}$). In contrast glutathione concentrations were significantly raised—270 (32) $\mu\text{g}/\text{ml}$ in patients with angina ($p < 0.01$), 292 (30) $\mu\text{g}/\text{ml}$ in claudication ($p < 0.04$), 208 (17) $\mu\text{g}/\text{ml}$ in controls. All patients with angina had important double or triple vessel disease and positive exercise tests. There was no significant change in superoxide dismutase and glutathione concentrations during exercise induced myocardial ischaemia.

These results suggest that these markers of excessive free radical production may define patients with vascular disease affecting the coronary and peripheral circulation.

³¹P nuclear magnetic resonance evaluation of skeletal muscle metabolism during exercise in congestive heart failure

B Massie, M Conway, R Yonge, S Frostick,

B Rajagopalan, G K Radda

Department of Biochemistry and Medicine, University of Oxford

In patients with congestive heart failure (CHF) the severity of exercise intolerance correlates poorly with central haemodynamic abnormalities. This suggests that the pathophysiology may be due to alterations in skeletal muscle metabolism or muscle blood flow. To study the mechanism of exercise impairment in CHF, we performed ³¹P magnetic resonance spectroscopy (MRS) in nine male patients (aged 42–62) with CHF due to ischaemic cardiomyopathy (6) and primary myocardial disease (3). Their mean ejection fraction was 16 (3)% and their maximum exercise tolerance ranged from 25 to 100 W. A 1.89 tesla, 20 cm bore magnet operating at 32.5 MHz for ³¹P was used with a surface coil over the flexor digitorum superficialis muscle. A previously standardised exercise protocol was used in which patients squeeze a rubber bulb at a rate of 22/min against a pressure of 100 torr for 5 min, followed by 300 torr for 2.5 min. Serial 32 scan spectra were obtained at 1.2 min intervals and analysed for pH, phosphocreatine (PCr), and inorganic phosphate (Pi). The rate of phosphate utilisation was followed as the ratio of PCr:(PCr + Pi).

Compared with 18 controls (aged 20–80) the CHF patients had similar resting pH (7.00 (0.03)) and PCr ratios (0.88 (0.03) vs 0.90 (0.02)). During exercise pH fell more rapidly in the patients and remained lower (6.40 (0.27) vs 6.86 (0.10) at 100 torr, $p < 0.001$; 6.44 (0.21) vs 6.68 (0.23) at 300 torr, $p < 0.02$). The PCr ratio fell faster at 100 torr (to 0.33 (0.15) vs 0.49 (0.14), $p < 0.02$) but at 300 torr reached a comparable level albeit with more work from the controls. Unlike the controls, five of the nine CHF patients developed double Pi peaks indicating the presence of at least two populations of muscle fibres with differing metabolic responses to exercise. These findings indicate that in CHF patients, skeletal muscle exhibits metabolic abnormalities during exercise which may be consistent with impaired nutritive blood flow or intrinsic alterations in cellular energetics.

Biochemical changes during repeated occlusion and reperfusion of a coronary artery in the rabbit: a ³¹P magnetic resonance spectroscopy study

B Rajagopalan, J Ramsey, E Harmsen, P Bore, G K Radda

Departments of Biochemistry, Anaesthetics, and Nuffield Department of Medicine, University of Oxford

Recanalisation of occluded coronary arteries is now an established therapeutic manoeuvre but the metabolic effects of reperfusion of the ischaemic myocardium are less well understood. We used ^{31}P magnetic resonance spectroscopy (MRS) to follow serially the metabolic effects of repeated myocardial ischaemia and reperfusion in six anaesthetised ventilated open chest rabbits. A 16 mm surface coil was placed on the lateral surface of the left ventricle and an adjustable snare was placed round a branch of the left coronary artery. Spectra were obtained in an Oxford Instruments 1.89 tesla 20 cm bore magnet. Changes in phosphocreatine (PCr), ATP, and inorganic phosphate + 2–3 diphosphoglycerate were measured from peak areas and pH from the chemical shift of inorganic phosphate. Spectra were obtained during a control period, during 15 min of total occlusion of the coronary artery, and after reperfusion. After allowing 45 min for recovery, the protocol was repeated. After occlusion, PCr fell rapidly in the first 7.5 min to 69% of control and remained depressed for the remaining ischaemic period. The pH fell from control to between 6.3–6.5. The ATP

did not change for the first 7.5 min, but fell to 90% of control during the second 7.5 min. When the vessel was reperfused, PCr returned to 103% of control within the first 10 min. In two animals ATP showed partial recovery, but in four it remained depressed or fell further. Arterial blood pressure fell by 10% during ischaemia and showed recovery to near control values after reperfusion. The peak areas immediately preceding the occlusion were used as control values and the magnitude and time course of changes after the second occlusion were similar to those that followed the first occlusion.

Unlike perfused hearts, in this in vivo model of regional ischaemia PCr fell precipitously to be followed by a fall in ATP. During reperfusion, PCr recovered while ATP remained depressed or fell further in four animals. This loss of ATP may contribute to the loss of function seen after repeated periods of ischaemia (the stunned myocardium). In summary, it is possible to follow serially the metabolic changes in repeated periods of ischaemia, and this should allow the study of models of reperfusion injury and pharmacological interventions.